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(71) Applicant *(for all designated States except US)*: GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BOUGUELERET, Lydie [FR/FR]; 108, avenue Victor Hugo, F-92170 Vanves (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue Victorine, F-94100 Saint-Maur (FR). DUMAS MILNE EDWARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, F-75006 Paris (FR).

(74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).

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(54) Title: EXTENDED cDNAs FOR SECRETED PROTEINS

(57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

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EXTENDED cDNAS for secreted proteins

The present application relates to extended cDNAs which were disclosed in several United States Provisional Patent Applications. Table I lists the SEQ ID Nos. of the extended cDNAs in the present application, the SEQ ID Nos. of the identical or nearly identical extended cDNAs in the provisional applications, and the identities of the provisional applications in which the extended cDNAs were disclosed.

Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized. Cloning vectors such as yeast artificial chromosomes (YACs) and bacterial artificial chromosomes (BACs) are able to accept DNA inserts ranging from 300 to 1000 kilobases (kb) or 100-400 kb in length respectively, thereby facilitating the manipulation and ordering of DNA sequences distributed over great distances on the human chromosomes. Automated DNA sequencing machines permit the rapid sequencing of human genes. Bioinformatics software enables the comparison of nucleic acid and protein sequences, thereby assisting in the characterization of human gene products.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bio-informatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bio-informatics software may mischaracterize the genomic sequences obtained. Thus, the software may produce false positives in which non-coding DNA is mischaracterized as coding DNA or false negatives in which coding DNA is mislabeled as non-coding DNA.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach, sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include

portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters.

In the past, the short EST sequences which could be used to isolate or purify extended cDNAs were often obtained from oligo-dT primed cDNA libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical techniques for obtaining cDNAs, are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs. (Adams et al., *Nature* 377:174, 1996, Hillier et al., *Genome Res.* 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported sequences typically correspond to coding sequences and do not include the full 5' untranslated region of the mRNA from which the cDNA is derived. Such incomplete sequences may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there is a need to obtain sequences derived from the 5' ends of mRNAs which can be used to obtain extended cDNAs which may include the 5' sequences contained in the 5' ESTs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. Of the 50,000-100,000 protein coding genes, those genes encoding proteins which are secreted from the cell in which they are synthesized, as well as the secreted proteins themselves, are particularly valuable as potential therapeutic agents. Such proteins are often involved in cell to cell communication and may be responsible for producing a clinically relevant response in their target cells.

In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon-α, interferon-β, interferon-γ, and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy induced neutropenia and multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a particularly valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

In addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are encoded by the signal sequences located at the 5' ends of the coding sequences of genes encoding secreted proteins. Because these signal peptides will direct the extracellular secretion of any protein to which they are operably linked, the signal sequences may be exploited to direct the efficient secretion of any protein by operably linking the signal sequences to a gene encoding the protein for which secretion is desired. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cell in which it is produced. Signal sequences encoding signal peptides

also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify and characterize the 5' portions of the genes for secretory proteins which encode signal peptides.

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches have been developed to isolate human promoters. One of them consists of making a CpG island library (Cross, S.H. et al., Purification of CpG Islands using a Methylated DNA Binding Column, Nature Genetics 6: 236-244 (1994)). The second consists of isolating human genomic DNA sequences containing SpeI binding sites by the use of SpeI binding protein. (Mortlock et al., *Genome Res.* 6:327-335, 1996). Both of these approaches have their limits due to a lack of specificity or of comprehensiveness.

5' ESTs and extended cDNAs obtainable therefrom may be used to efficiently identify and isolate upstream regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. (Theil *et al., BioFactors* 4:87-93, (1993). Once identified and characterized, these regulatory regions may be utilized in gene therapy or protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce, or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of secretory protein genes or extended cDNAs which include sequences adjacent to the sequences of the ESTs may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes encoding secretory proteins.

Summary of the Invention

The present invention relates to purified, isolated, or recombinant extended cDNAs which encode secreted proteins or fragments thereof. Preferably, the purified, isolated or recombinant cDNAs contain the entire open reading frame of their corresponding mRNAs, including a start codon and a stop codon. For example, the extended cDNAs may include nucleic acids encoding the signal peptide as well as the mature protein. Alternatively, the extended cDNAs may contain a fragment of the open reading frame. In some embodiments, the fragment may encode only the sequence of the mature protein. Alternatively, the fragment may encode only a portion of the mature protein. A further aspect of the present invention is a nucleic acid which encodes the signal peptide of a secreted protein.

The present extended cDNAs were obtained using ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. As used herein the terms "EST" or "5' EST" refer to the short cDNAs which were used to obtain the extended cDNAs of the present invention. As used herein, the term "extended cDNA" refers to the cDNAs which include sequences adjacent to the 5' EST used to obtain them. The extended cDNAs may contain all or a

portion of the sequence of the EST which was used to obtain them. The term "corresponding mRNA" refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual extended cDNA clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The extended cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 10^4-10^6 fold purification of the native message. Purification of starting material or natural material to at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the extended cDNA is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the extended cDNAs will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched extended cDNAs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched extended cDNAs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched extended cDNAs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. "Stringent", "moderate," and "low" hybridization conditions are as defined in Example 29.

Unless otherwise indicated, a "complementary" sequence is fully complementary. Thus, extended cDNAs encoding secreted polypeptides or fragments thereof which are present in cDNA libraries in which one or more extended cDNAs encoding secreted polypeptides or fragments thereof make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant extended cDNAs" as defined herein. Likewise, extended cDNAs encoding secreted polypeptides or fragments thereof which are in a population of plasmids in which one or more extended cDNAs of the present invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are " enriched recombinant extended cDNAs" as defined herein. However, extended

cDNAs encoding secreted polypeptides or fragments thereof which are in cDNA libraries in which the extended cDNAs encoding secreted polypeptides or fragments thereof constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in which backbone molecules having a cDNA insert encoding a secreted polypeptide are extremely rare, are not "enriched recombinant extended cDNAs."

In particular, the present invention relates to extended cDNAs which were derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

Extended cDNAs encoding secreted proteins may include nucleic acid sequences, called signal sequences, which encode signal peptides which direct the extracellular secretion of the proteins encoded by the extended cDNAs. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across the cell membrane.

The extended cDNAs of the present invention have several important applications. For example, they may be used to express the entire secreted protein which they encode. Alternatively, they may be used to express portions of the secreted protein. The portions may comprise the signal peptides encoded by the extended cDNAs or the mature proteins encoded by the extended cDNAs (i.e. the proteins generated when the signal peptide is cleaved off). The portions may also comprise polypeptides having at least 10 consecutive amino acids encoded by the extended cDNAs. Alternatively, the portions may comprise at least 15 consecutive amino acids encoded by the extended cDNAs. In some embodiments, the portions may comprise at least 25 consecutive amino acids encoded by the extended cDNAs. In other embodiments, the portions may comprise at least 40 amino acids encoded by the extended cDNAs.

Antibodies which specifically recognize the entire secreted proteins encoded by the extended cDNAs or fragments thereof having at least 10 consecutive amino acids, at least 15 consecutive amino acids, at least 25 consecutive amino acids, or at least 40 consecutive amino acids may also be obtained as described below. Antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides encoded by the extended cDNAs may also be obtained.

In some embodiments, the extended cDNAs include the signal sequence. In other embodiments, the extended cDNAs may include the full coding sequence for the mature protein (i.e. the protein generated when the signal polypeptide is cleaved off). In addition, the extended cDNAs may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene expression. As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating or controlling a variety of human conditions. The extended cDNAs may also be used to obtain the corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes mRNA which includes the sequence of one of the strands of the extended cDNA in which thymidine residues in the sequence of the extended cDNA are replaced by uracil residues in the mRNA.

The extended cDNAs or genomic DNAs obtained therefrom may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal expression of the genes corresponding to the extended cDNAs. In addition, the present invention is useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a protein of interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired proteins.

The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the extended cDNAs such as promoters or upstream regulatory sequences.

In addition, the present invention may also be used for gene therapy to control or treat genetic diseases. Signal peptides may also be fused to heterologous proteins to direct their extracellular secretion.

One embodiment of the present invention is a purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. In one aspect of this embodiment, the nucleic acid comprises at least 15, 25, 30, 40, 50, 75, or 100 consecutive bases of one of the sequences of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. The nucleic acid may be a recombinant nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEQ ID NOs: 40-140 and 242-377. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising the full coding sequences of one of SEQ ID NOs: 40-140 and 242-377, wherein the full coding sequence optionally comprises the sequence encoding signal peptide as well as the sequence encoding mature protein. In a preferred embodiment, the isolated or purified nucleic acid comprises the full coding sequence of one of SEQ ID Nos. 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377 wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

A further embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode a mature protein. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

Yet another embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode the signal peptide. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of SEQ ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a mature protein included in one of the sequences of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is a purified or isolated protein comprising the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is a purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the purified or isolated polypeptide comprises at least 15, 20, 25, 35, 50, 75, 100, 150 or 200 consecutive

amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In still another aspect, the purified or isolated polypeptide comprises at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is an isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

A further embodiment of the present invention is a method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-377, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the protein encoded by said cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a protein obtainable by the method described in the preceding paragraph.

Another embodiment of the present invention is a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEQ ID NO: 40-140 and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a mature protein obtainable by the method described in the preceding paragraph.

In a preferred embodiment, the above method comprises a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEQ ID NO: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEQ ID NO:

40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the full coding sequences of one of SEQ ID NOs: 40-140 and 242-377, wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode a mature protein which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode the signal peptide which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID Nos.: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide.

Another embodiment of the present invention is a purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the antibody is capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an array of cDNAs or fragments thereof of at least 15 nucleotides in length which includes at least one of the sequences of SEQ ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides. In one aspect of this embodiment, the array includes at least two of the sequences of SEQ ID NOs: 40-140 and 242-377, the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides. In another aspect of this embodiment, the array includes at least five of the sequences of SEQ ID NOs: 40-140 and 242-377, the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides.

A further embodiment of the invention encompasses purified polynucleotides comprising an insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI or a fragment thereof comprising a contiguous span of at least 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 nucleotides of said insert. An additional embodiment of the invention encompasses purified polypeptides which comprise, consist of, or consist essentially of an amino acid sequence encoded by the insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI, as well as polypeptides which comprise a fragment of said amino acid sequence consisting of a signal peptide, a mature protein, or a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids encoded by said insert.

An additional embodiment of the invention encompasses purified polypeptides which comprise a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids of SEQ ID NOs: 158, 174, 175, 196, 226, 231, 232, wherein said contiguous span comprises at least one of the amino acid positions which was not shown to be identical to a public sequence in any of Figures 11 to 15. Also encompassed by the invention are purified polynuculeotides encoding said polypeptides.

Brief Description of the Drawings

Figure 1 is a summary of a procedure for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived.

Figure 2 is an analysis of the 43 amino terminal amino acids of all human SwissProt proteins to determine the frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Figure 3 shows the distribution of von Heijne scores for 5' ESTs in each of the categories described herein and the probability that these 5' ESTs encode a signal peptide.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the categories described herein were obtained.

Figure 6 illustrates a method for obtaining extended cDNAs.

Figure 7 is a map of pED6dpc2. pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SSt cDNAs are cloned between EcoRI and NotI. PED vectors are described in Kaufman et al. (1991), NAR 19: 4485-4490.

Figure 8 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags.

Figure 9 describes the transcription factor binding sites present in each of these promoters.

Figure 10 is an alignment of the protein of SEQ ID NO: 217 with the human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEQ ID NO: 516).

Figure 11 is an alignment of the proteins of SEQ ID NOs: 174, 175 and 232 with a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517).

Figure 12 is an alignment of the protein of SEQ ID NO: 231 with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515).

Figure 13 is an alignment of the protein of SEQ ID NO: 196 with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518).

Figure 14 is an alignment of the protein of SEQ ID NOs: 158 with the murine subunit 7a of the COP9 complex (Genbank accession number AF071316, SEQ ID NO: 519).

Figure 15 is an alignment of the protein of SEQ ID NO: 226 with the bovine subunit B14.5B of the NADH-ubiquinone oxidureductase complex (Arizmendi *et al, FEBS Lett.,* 313 : 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514).

Detailed Description of the Preferred Embodiment

I. Obtaining 5′ ESTs

The present extended cDNAs were obtained using 5′ ESTs which were isolated as described below.

A. Chemical Methods for Obtaining mRNAs having Intact 5′ Ends

In order to obtain the 5′ ESTs used to obtain the extended cDNAs of the present invention, mRNAs having intact 5′ ends must be obtained. Currently, there are two approaches for obtaining such mRNAs. One of these approaches is a chemical modification method involving derivatization of the 5′ ends of the mRNAs and selection of the derivatized mRNAs. The 5′ ends of eucaryotic mRNAs possess a structure referred to as a "cap" which comprises a guanosine methylated at the 7 position. The cap is joined to the first transcribed base of the mRNA by a 5′, 5′-triphosphate bond. In some instances, the 5′ guanosine is methylated in both the 2 and 7 positions. Rarely, the 5′ guanosine is trimethylated at the 2, 7 and 7 positions. In the chemical method for obtaining mRNAs having intact 5′ ends, the 5′ cap is specifically derivatized and coupled to a reactive group on an immobilizing substrate. This specific derivatization is based on the fact that only the ribose linked to the methylated guanosine at the 5′ end of the mRNA and the ribose linked to the base at the 3′ terminus of the mRNA, possess 2′, 3′-cis diols. Optionally, where the 3′ terminal ribose has a 2′, 3′-cis diol, the 2′, 3′-cis diol at the 3′ end may be chemically modified, substituted, converted, or eliminated, leaving only the ribose linked to the methylated guanosine at the 5′ end of the mRNA with a 2′, 3′-cis diol. A variety of techniques are available for eliminating the 2′, 3′-cis diol on the 3′ terminal ribose. For example, controlled alkaline hydrolysis may be used to generate mRNA fragments in which the 3′ terminal ribose is a 3′-phosphate, 2′-phosphate or (2′, 3′)-cyclophosphate. Thereafter, the fragment which includes the original 3′ ribose may be eliminated from the mixture through chromatography on an oligo-dT column. Alternatively, a base which lacks the 2′, 3′-cis diol

may be added to the 3′ end of the mRNA using an RNA ligase such as T4 RNA ligase. Example 1 below describes a method for ligation of pCp to the 3′ end of messenger RNA.

EXAMPLE 1

Ligation of the Nucleoside Diphosphate pCp to the 3′ End of Messenger RNA

1 μg of RNA was incubated in a final reaction medium of 10 μl in the presence of 5 U of T_4 phage RNA ligase in the buffer provided by the manufacturer (Gibco - BRL), 40 U of the RNase inhibitor RNasin (Promega) and, 2 μl of ^{32}pCp (Amersham #PB 10208).

The incubation was performed at 37°C for 2 hours or overnight at 7-8°C.

Following modification or elimination of the 2′, 3′-cis diol at the 3′ ribose, the 2′, 3′-cis diol present at the 5′ end of the mRNA may be oxidized using reagents such as $NaBH_4$, $NaBH_3CN$, or sodium periodate, thereby converting the 2′, 3′-cis diol to a dialdehyde. Example 2 describes the oxidation of the 2′, 3′-cis diol at the 5′ end of the mRNA with sodium periodate.

EXAMPLE 2

Oxidation of 2′, 3′-cis diol at the 5′ End of the mRNA

0.1 OD unit of either a capped oligoribonucleotide of 47 nucleotides (including the cap) or an uncapped oligoribonucleotide of 46 nucleotides were treated as follows. The oligoribonucleotides were produced by in vitro transcription using the transcription kit "AmpliScribe T7" (Epicentre Technologies). As indicated below, the DNA template for the RNA transcript contained a single cytosine. To synthesize the uncapped RNA, all four NTPs were included in the in vitro transcription reaction. To obtain the capped RNA, GTP was replaced by an analogue of the cap, m7G(5′)ppp(5′)G. This compound, recognized by polymerase, was incorporated into the 5′ end of the nascent transcript during the step of initiation of transcription but was not capable of incorporation during the extension step. Consequently, the resulting RNA contained a cap at its 5′ end. The sequences of the oligoribonucleotides produced by the in vitro transcription reaction were:

+Cap:

5′m7GpppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3′ (SEQ ID NO:1)

-Cap:

5′-pppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3′ (SEQ ID NO:2)

The oligoribonucleotides were dissolved in 9 μl of acetate buffer (0.1 M sodium acetate, pH 5.2) and 3 μl of freshly prepared 0.1 M sodium periodate solution. The mixture was incubated for 1 hour in the dark at 4°C or room temperature. Thereafter, the reaction was stopped by adding 4 μl of 10% ethylene glycol. The product was ethanol precipitated, resuspended in 10μl or more of water or appropriate buffer and dialyzed against water.

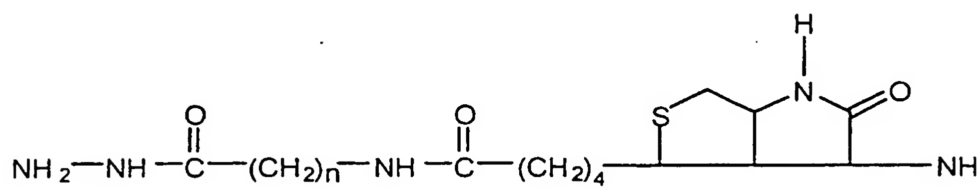
The resulting aldehyde groups may then be coupled to molecules having a reactive amine group, such as hydrazine, carbazide, thiocarbazide or semicarbazide groups, in order to facilitate enrichment of the 5′ ends of the mRNAs. Molecules having reactive amine groups which are suitable for use in selecting mRNAs having intact 5′ ends

include avidin, proteins, antibodies, vitamins, ligands capable of specifically binding to receptor molecules, or oligonucleotides. Example 3 below describes the coupling of the resulting dialdehyde to biotin.

EXAMPLE 3

Coupling of the Dialdehyde with Biotin

The oxidation product obtained in Example 2 was dissolved in 50 μl of sodium acetate at a pH of between 5 and 5.2 and 50 μl of freshly prepared 0.02 M solution of biotin hydrazide in a methoxyethanol/water mixture (1:1) of formula:



In the compound used in these experiments, n=5. However, it will be appreciated that other commercially available hydrazides may also be used, such as molecules of the formula above in which n varies from 0 to 5.

The mixture was then incubated for 2 hours at 37°C. Following the incubation, the mixture was precipitated with ethanol and dialyzed against distilled water.

Example 4 demonstrates the specificity of the biotinylation reaction.

EXAMPLE 4

Specificity of Biotinylation

The specificity of the biotinylation for capped mRNAs was evaluated by gel electrophoresis of the following samples:

Sample 1. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2 and labeled with ^{32}pCp as described in Example 1.

Sample 2. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2, labeled with ^{32}pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Sample 3. The 47 nucleotide capped in vitro transcript prepared as in Example 2 and labeled with ^{32}pCp as described in Example 1.

Sample 4. The 47 nucleotide capped in vitro transcript prepared as in Example 2, labeled with ^{32}pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Samples 1 and 2 had indentical migration rates, demonstrating that the uncapped RNAs were not oxidized and biotinylated. Sample 3 migrated more slowly than Samples 1 and 2, while Sample 4 exhibited the slowest migration.

The difference in migration of the RNAs in Samples 3 and 4 demonstrates that the capped RNAs were specifically biotinylated.

In some cases, mRNAs having intact 5' ends may be enriched by binding the molecule containing a reactive amine group to a suitable solid phase substrate such as the inside of the vessel containing the mRNAs, magnetic beads, chromatography matrices, or nylon or nitrocellulose membranes. For example, where the molecule having a reactive amine group is biotin, the solid phase substrate may be coupled to avidin or streptavidin. Alternatively, where the molecule having the reactive amine group is an antibody or receptor ligand, the solid phase substrate may be coupled to the cognate antigen or receptor. Finally, where the molecule having a reactive amine group comprises an oligonucleotide, the solid phase substrate may comprise a complementary oligonucleotide.

The mRNAs having intact 5' ends may be released from the solid phase following the enrichment procedure. For example, where the dialdehyde is coupled to biotin hydrazide and the solid phase comprises streptavidin, the mRNAs may be released from the solid phase by simply heating to 95 degrees Celsius in 2% SDS. In some methods, the molecule having a reactive amine group may also be cleaved from the mRNAs having intact 5' ends following enrichment. Example 5 describes the capture of biotinylated mRNAs with streptavidin coated beads and the release of the biotinylated mRNAs from the beads following enrichment.

EXAMPLE 5

Capture and Release of Biotinylated mRNAs Using Strepatividin Coated Beads

The streptavidin-coated magnetic beads were prepared according to the manufacturer's instructions (CPG Inc., USA). The biotinylated mRNAs were added to a hybridization buffer (1.5 M NaCl, pH 5 - 6). After incubating for 30 minutes, the unbound and nonbiotinylated material was removed. The beads were washed several times in water with 1% SDS. The beads obtained were incubated for 15 minutes at 95°C in water containing 2% SDS.

Example 6 demonstrates the efficiency with which biotinylated mRNAs were recovered from the streptavidin coated beads.

EXAMPLE 6

Efficiency of Recovery of Biotinylated mRNAs

The efficiency of the recovery procedure was evaluated as follows. RNAs were labeled with ^{32}pCp, oxidized, biotinylated and bound to streptavidin coated beads as described above. Subsequently, the bound RNAs were incubated for 5, 15 or 30 minutes at 95°C in the presence of 2% SDS.

The products of the reaction were analyzed by electrophoresis on 12% polyacrylamide gels under denaturing conditions (7 M urea). The gels were subjected to autoradiography. During this manipulation, the hydrazone bonds were not reduced.

Increasing amounts of nucleic acids were recovered as incubation times in 2% SDS increased, demonstrating that biotinylated mRNAs were efficiently recovered.

In an alternative method for obtaining mRNAs having intact 5′ ends, an oligonucleotide which has been derivatized to contain a reactive amine group is specifically coupled to mRNAs having an intact cap. Preferably, the 3′ end of the mRNA is blocked prior to the step in which the aldehyde groups are joined to the derivatized oligonucleotide, as described above, so as to prevent the derivatized oligonucleotide from being joined to the 3′ end of the mRNA. For example, pCp may be attached to the 3′ end of the mRNA using T4 RNA ligase. However, as discussed above, blocking the 3′ end of the mRNA is an optional step. Derivatized oligonucleotides may be prepared as described below in Example 7.

EXAMPLE 7

Derivatization of the Oligonucleotide

An oligonucleotide phosphorylated at its 3′ end was converted to a 3′ hydrazide in 3′ by treatment with an aqueous solution of hydrazine or of dihydrazide of the formula $H_2N(R1)NH_2$ at about 1 to 3 M, and at pH 4.5, in the presence of a carbodiimide type agent soluble in water such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide at a final concentration of 0.3 M at a temperature of 8°C overnight.

The derivatized oligonucleotide was then separated from the other agents and products using a standard technique for isolating oligonucleotides.

As discussed above, the mRNAs to be enriched may be treated to eliminate the 3′ OH groups which may be present thereon. This may be accomplished by enzymatic ligation of sequences lacking a 3′ OH, such as pCp, as described above in Example 1. Alternatively, the 3′ OH groups may be eliminated by alkaline hydrolysis as described in Example 8 below.

EXAMPLE 8

Alkaline Hydrolysis of mRNA

The mRNAs may be treated with alkaline hydrolysis as follows. In a total volume of 100μl of 0.1N sodium hydroxide, 1.5μg mRNA is incubated for 40 to 60 minutes at 4°C. The solution is neutralized with acetic acid and precipitated with ethanol.

Following the optional elimination of the 3′ OH groups, the diol groups at the 5′ ends of the mRNAs are oxidized as described below in Example 9.

EXAMPLE 9

Oxidation of Diols

Up to 1 OD unit of RNA was dissolved in 9 μl of buffer (0.1 M sodium acetate, pH 6-7 or water) and 3 μl of freshly prepared 0.1 M sodium periodate solution. The reaction was incubated for 1 h in the dark at 4°C or room temperature. Following the incubation, the reaction was stopped by adding 4 μl of 10% ethylene glycol. Thereafter the mixture was incubated at room temperature for 15 minutes. After ethanol precipitation, the product was resuspended in 10μl or more of water or appropriate buffer and dialyzed against water.

Following oxidation of the diol groups at the 5' ends of the mRNAs, the derivatized oligonucleotide was joined to the resulting aldehydes as described in Example 10.

EXAMPLE 10

Reaction of Aldehydes with Derivatized Oligonucleotides

The oxidized mRNA was dissolved in an acidic medium such as 50 μl of sodium acetate pH 4-6. 50 μl of a solution of the derivatized oligonucleotide was added such that an mRNA:derivatized oligonucleotide ratio of 1:20 was obtained and mixture was reduced with a borohydride. The mixture was allowed to incubate for 2 h at 37°C or overnight (14 h) at 10°C. The mixture was ethanol precipitated, resuspended in 10μl or more of water or appropriate buffer and dialyzed against distilled water. If desired, the resulting product may be analyzed using acrylamide gel electrophoresis, HPLC analysis, or other conventional techniques.

Following the attachment of the derivatized oligonucleotide to the mRNAs, a reverse transcription reaction may be performed as described in Example 11 below.

EXAMPLE 11

Reverse Transcription of mRNAs

An oligodeoxyribonucleotide was derivatized as follows. 3 OD units of an oligodeoxyribonucleotide of sequence ATCAAGAATTCGCACGAGACCATTA (SEQ ID NO:3) having 5'-OH and 3'-P ends were dissolved in 70 μl of a 1.5 M hydroxybenzotriazole solution, pH 5.3, prepared in dimethylformamide/water (75:25) containing 2 μg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The mixture was incubated for 2 h 30 min at 22°C. The mixture was then precipitated twice in $LiClO_4$/acetone. The pellet was resuspended in 200 μl of 0.25 M hydrazine and incubated at 8°C from 3 to 14 h. Following the hydrazine reaction, the mixture was precipitated twice in $LiClO_4$/acetone.

The messenger RNAs to be reverse transcribed were extracted from blocks of placenta having sides of 2 cm which had been stored at -80°C. The mRNA was extracted using conventional acidic phenol techniques. Oligo-dT chromatography was used to purify the mRNAs. The integrity of the mRNAs was checked by Northern-blotting.

The diol groups on 7 μg of the placental mRNAs were oxidized as described above in Example 9. The derivatized oligonucleotide was joined to the mRNAs as described in Example 10 above except that the precipitation step was replaced by an exclusion chromatography step to remove derivatized oligodeoxyribonucleotides which were not joined to mRNAs. Exclusion chromatography was performed as follows:

10 ml of AcA34 (BioSepra#230151) gel were equilibrated in 50 ml of a solution of 10 mM Tris pH 8.0, 300 mM NaCl, 1 mM EDTA, and 0.05% SDS. The mixture was allowed to sediment. The supernatant was eliminated and the gel was resuspended in 50 ml of buffer. This procedure was repeated 2 or 3 times.

A glass bead (diameter 3 mm) was introduced into a 2 ml disposable pipette (length 25 cm). The pipette was filled with the gel suspension until the height of the gel stabilized at 1 cm from the top of the pipette. The column was then equilibrated with 20 ml of equilibration buffer (10 mM Tris HCl pH 7.4, 20 mM NaCl).

10 μl of the mRNA which had been reacted with the derivatized oligonucleotide were mixed in 39 μl of 10 mM urea and 2 μl of blue-glycerol buffer, which had been prepared by dissolving 5 mg of bromophenol blue in 60% glycerol (v/v), and passing the mixture through a filter with a filter of diameter 0.45 μm.

The column was loaded. As soon as the sample had penetrated, equilibration buffer was added. 100 μl fractions were collected. Derivatized oligonucleotide which had not been attached to mRNA appeared in fraction 16 and later fractions. Fractions 3 to 15 were combined and precipitated with ethanol.

The mRNAs which had been reacted with the derivatized oligonucleotide were spotted on a nylon membrane and hybridized to a radioactive probe using conventional techniques. The radioactive probe used in these hybridizations was an oligodeoxyribonucleotide of sequence TAATGGTCTCGTGCGAATTCTTGAT (SEQ ID NO:4) which was anticomplementary to the derivatized oligonucleotide and was labeled at its 5' end with ^{32}P. 1/10th of the mRNAs which had been reacted with the derivatized oligonucleotide was spotted in two spots on the membrane and the membrane was visualized by autoradiography after hybridization of the probe. A signal was observed, indicating that the derivatized oligonucleotide had been joined to the mRNA.

The remaining 9/10 of the mRNAs which had been reacted with the derivatized oligonucleotide was reverse transcribed as follows. A reverse transcription reaction was carried out with reverse transcriptase following the manufacturer's instructions. To prime the reaction, 50 pmol of nonamers with random sequence were used.

A portion of the resulting cDNA was spotted on a positively charged nylon membrane using conventional methods. The cDNAs were spotted on the membrane after the cDNA:RNA heteroduplexes had been subjected to an alkaline hydrolysis in order to eliminate the RNAs. An oligonucleotide having a sequence identical to that of the derivatized oligonucleotide was labeled at its 5' end with ^{32}P and hybridized to the cDNA blots using conventional techniques. Single-stranded cDNAs resulting from the reverse transcription reaction were spotted on the membrane. As controls, the blot contained 1 pmol, 100 fmol, 50 fmol, 10 fmol and 1 fmol respectively of a control oligodeoxyribonucleotide of sequence identical to that of the derivatized oligonucleotide. The signal observed in the spots containing the cDNA indicated that approximately 15 fmol of the derivatized oligonucleotide had been reverse transcribed.

These results demonstrate that the reverse transcription can be performed through the cap and, in particular, that reverse transcriptase crosses the 5'-P-P-P-5' bond of the cap of eukaryotic messenger RNAs.

The single stranded cDNAs obtained after the above first strand synthesis were used as template for PCR reactions. Two types of reactions were carried out. First, specific amplification of the mRNAs for the alpha globin, dehydrogenase, pp15 and elongation factor E4 were carried out using the following pairs of oligodeoxyribonucleotide primers.

alpha-globin

GLO-S: CCG ACA AGA CCA ACG TCA AGG CCG C (SEQ ID NO:5)

GLO-As: TCA CCA GCA GGC AGT GGC TTA GGA G 3' (SEQ ID NO:6)

dehydrogenase

3 DH-S: AGT GAT TCC TGC TAC TTT GGA TGG C (SEQ ID NO:7)

3 DH-As: GCT TGG TCT TGT TCT GGA GTT TAG A (SEQ ID NO:8)

pp15

PP15-S: TCC AGA ATG GGA GAC AAG CCA ATT T (SEQ ID NO:9)

PP15-As: AGG GAG GAG GAA ACA GCG TGA GTC C (SEQ ID NO:10)

Elongation factor E4

EFA1-S: ATG GGA AAG GAA AAG ACT CAT ATC A (SEQ ID NO:11)

EF1A-As: AGC AGC AAC AAT CAG GAC AGC ACA G (SEQ ID NO:12)

Non specific amplifications were also carried out with the antisense (_As) oligodeoxyribonucleotides of the pairs described above and a primer chosen from the sequence of the derivatized oligodeoxyribonucleotide (ATCAAGAATTCGCACGAGACCATTA) (SEQ ID NO:13).

A 1.5% agarose gel containing the following samples corresponding to the PCR products of reverse transcription was stained with ethidium bromide. (1/20th of the products of reverse transcription were used for each PCR reaction).

Sample 1: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the presence of cDNA.

Sample 2: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the absence of added cDNA.

Sample 3: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the presence of cDNA.

Sample 4: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the absence of added cDNA.

Sample 5: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the presence of cDNA.

Sample 6: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the absence of added cDNA.

Sample 7: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the presence of added cDNA.

Sample 8: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the absence of added cDNA.

In Samples 1, 3, 5 and 7, a band of the size expected for the PCR product was observed, indicating the presence of the corresponding sequence in the cDNA population.

PCR reactions were also carried out with the antisense oligonucleotides of the globin and dehydrogenase primers (SEQ ID NOs 6 and 8) and an oligonucleotide whose sequence corresponds to that of the derivatized

oligonucleotide. The presence of PCR products of the expected size in the samples corresponding to samples 1 and 3 above indicated that the derivatized oligonucleotide had been incorporated.

The above examples summarize the chemical procedure for enriching mRNAs for those having intact 5′ ends. Further detail regarding the chemical approaches for obtaining mRNAs having intact 5′ ends are disclosed in International Application No. WO96/34981, published November 7, 1996.

Strategies based on the above chemical modifications to the 5′ cap structure may be utilized to generate cDNAs which have been selected to include the 5′ ends of the mRNAs from which they are derived. In one version of such procedures, the 5′ ends of the mRNAs are modified as described above. Thereafter, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5′ end of the mRNA. Single stranded RNAs are eliminated to obtain a population of cDNA/mRNA heteroduplexes in which the mRNA includes an intact 5′ end. The resulting heteroduplexes may be captured on a solid phase coated with a molecule capable of interacting with the molecule used to derivatize the 5′ end of the mRNA. Thereafter, the strands of the heteroduplexes are separated to recover single stranded first cDNA strands which include the 5′ end of the mRNA. Second strand cDNA synthesis may then proceed using conventional techniques. For example, the procedures disclosed in WO 96/34981 or in Carninci, P. et al. High-Efficiency Full-Length cDNA Cloning by Biotinylated CAP Trapper. **Genomics** 37:327-336 (1996) may be employed to select cDNAs which include the sequence derived from the 5′ end of the coding sequence of the mRNA.

Following ligation of the oligonucleotide tag to the 5′ cap of the mRNA, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5′ end of the mRNA. Following elimination of the RNA component of the resulting heteroduplex using standard techniques, second strand cDNA synthesis is conducted with a primer complementary to the oligonucleotide tag.

Figure 1 summarizes the above procedures for obtaining cDNAs which have been selected to include the 5′ ends of the mRNAs from which they are derived.

B. <u>Enzymatic Methods for Obtaining mRNAs having Intact 5′ Ends</u>

Other techniques for selecting cDNAs extending to the 5′ end of the mRNA from which they are derived are fully enzymatic. Some versions of these techniques are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'etude de la regulation de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EPO 625572 and Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994).

Briefly, in such approaches, isolated mRNA is treated with alkaline phosphatase to remove the phosphate groups present on the 5′ ends of uncapped incomplete mRNAs. Following this procedure, the cap present on full length mRNAs is enzymatically removed with a decapping enzyme such as T4 polynucleotide kinase or tobacco acid pyrophosphatase. An oligonucleotide, which may be either a DNA oligonucleotide or a DNA-RNA hybrid oligonucleotide having RNA at its 3′ end, is then ligated to the phosphate present at the 5′ end of the decapped mRNA using T4 RNA

ligase.. The oligonucleotide may include a restriction site to facilitate cloning of the cDNAs following their synthesis. Example 12 below describes one enzymatic method based on the doctoral thesis of Dumas.

EXAMPLE 12

Enzymatic Approach for Obtaining 5' ESTs

Twenty micrograms of PolyA+ RNA were dephosphorylated using Calf Intestinal Phosphatase (Biolabs). After a phenol chloroform extraction, the cap structure of mRNA was hydrolysed using the Tobacco Acid Pyrophosphatase (purified as described by Shinshi et al., Biochemistry 15: 2185-2190, 1976) and a hemi 5'DNA/RNA-3' oligonucleotide having an unphosphorylated 5' end, a stretch of adenosine ribophosphate at the 3' end, and an EcoRI site near the 5' end was ligated to the 5'P ends of mRNA using the T4 RNA ligase (Biolabs). Oligonucleotides suitable for use in this procedure are preferably 30-50 bases in length. Oligonucleotides having an unphosphorylated 5' end may be synthesized by adding a fluorochrome at the 5' end. The inclusion of a stretch of adenosine ribophosphates at the 3' end of the oligonucleotide increases ligation efficiency. It will be appreciated that the oligonucleotide may contain cloning sites other than EcoRI.

Following ligation of the oligonucleotide to the phosphate present at the 5' end of the decapped mRNA, first and second strand cDNA synthesis may be carried out using conventional methods or those specified in EPO 625,572 and Kato et al. Construction of a Human Full-Length cDNA Bank. **Gene** 150:243-250 (1994), and Dumas Milne Edwards, *supra*. The resulting cDNA may then be ligated into vectors such as those disclosed in Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994) or other nucleic acid vectors known to those skilled in the art using techniques such as those described in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989.

II. Characterization of 5' ESTs

The above chemical and enzymatic approaches for enriching mRNAs having intact 5' ends were employed to obtain 5' ESTs. First, mRNAs were prepared as described in Example 13 below.

EXAMPLE 13

Preparation of mRNA

Total human RNAs or PolyA+ RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as described below. The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski, P and Sacchi, N., **Analytical Biochemistry** 162:156-159, 1987). PolyA+ RNA was isolated from total RNA (LABIMO) by two passes of oligodT chromatography, as described by Aviv and Leder (Aviv, H. and Leder, P., **Proc. Natl. Acad. Sci. USA** 69:1408-1412, 1972) in order to eliminate ribosomal RNA.

The quality and the integrity of the poly A+ were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the PolyA+ mRNAs by ribosomal sequences was checked using RNAs blots and a probe derived from the sequence of the 28S RNA. Preparations of mRNAs with less

than 5% of ribosomal RNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed mRNAs was examined using PCR.

Following preparation of the mRNAs, the above described chemical and/or the enzymatic procedures for enriching mRNAs having intact 5' ends discussed above were employed to obtain 5' ESTs from various tissues. In both approaches an oligonucleotide tag was attached to the cap at the 5' ends of the mRNAs. The oligonucleotide tag had an EcoRI site therein to facilitate later cloning procedures.

Following attachment of the oligonucleotide tag to the mRNA by either the chemical or enzymatic methods, the integrity of the mRNA was examined by performing a Northern blot with 200-500ng of mRNA using a probe complementary to the oligonucleotide tag.

EXAMPLE 14

cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags using both the chemical and enzymatic methods, first strand cDNA synthesis was performed using reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of RNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

For both the chemical and the enzymatic methods, the second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5'end of the ligated oligonucleotide described in Example 12. Preferably, the primer is 20-25 bases in length. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

Following cDNA synthesis, the cDNAs were cloned into pBlueScript as described in Example 15 below.

EXAMPLE 15

Insertion of cDNAs into BlueScript

Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was used during cDNA synthesis, the EcoRI site present in the tag was the only site which was hemi-methylated. Consequently, only the EcoRI site in the oligonucleotide tag was susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra). Fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the SmaI and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

Clones containing the oligonucleotide tag attached were selected as described in Example 16 below.

EXAMPLE 16

Selection of Clones Having the Oligonucleotide Tag Attached Thereto

The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., **Gene** 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., **Biotechniques, 13**: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide described in Example 13. Preferably, the primer has a length of 20-25 bases. Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double stranded DNA using a DNA polymerase such as the ThermoSequenase obtained from Amersham Pharmacia Biotech. Alternatively, protocols such as the Gene Trapper kit (Gibco BRL) may be used. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated to typically rank between 90 and 98% using dot blot analysis.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

EXAMPLE 17

Sequencing of Inserts in Selected Clones

Plasmid inserts were first amplified by PCR on PE 9600 thermocyclers (Perkin-Elmer), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer, Applied Biosystems Division, Foster City, CA). Sequencing reactions were performed using PE 9600 thermocyclers (Perkin Elmer) with standard dye-primer chemistry and ThermoSequenase (Amersham Life Science). The primers used were either T7 or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer, reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with EtOH, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing Analysis Software, version 2.1.2.

The sequence data from the 44 cDNA libraries made as described above were transferred to a proprietary database, where quality control and validation steps were performed. A proprietary base-caller ("Trace"), working using a Unix system automatically flagged suspect peaks, taking into account the shape of the peaks, the inter-peak resolution, and the noise level. The proprietary base-caller also performed an automatic trimming. Any stretch of 25 or

fewer bases having more than 4 suspect peaks was considered unreliable and was discarded. Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case by case basis.

Thereafter, the sequences were transferred to the proprietary NETGENE™ Database for further analysis as described below.

Following sequencing as described above, the sequences of the 5' ESTs were entered in a proprietary database called NETGENE™ for storage and manipulation. It will be appreciated by those skilled in the art that the data could be stored and manipulated on any medium which can be read and accessed by a computer. Computer readable media include magnetically readable media, optically readable media, or electronically readable media. For example, the computer readable media may be a hard disc, a floppy disc, a magnetic tape, CD-ROM, RAM, or ROM as well as other types of other media known to those skilled in the art.

In addition, the sequence data may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the sequence data may be stored as text in a word processing file, such as MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE.

The computer readable media on which the sequence information is stored may be in a personal computer, a network, a server or other computer systems known to those skilled in the art. The computer or other system preferably includes the storage media described above, and a processor for accessing and manipulating the sequence data.

Once the sequence data has been stored it may be manipulated and searched to locate those stored sequences which contain a desired nucleic acid sequence or which encode a protein having a particular functional domain. For example, the stored sequence information may be compared to other known sequences to identify homologies, motifs implicated in biological function, or structural motifs.

Programs which may be used to search or compare the stored sequences include the MacPattern (EMBL), BLAST, and BLAST2 program series (NCBI), basic local alignment search tool programs for nucleotide (BLASTN) and peptide (BLASTX) comparisons (Altschul et al, **J. Mol. Biol. 215**: 403 (1990)) and FASTA (Pearson and Lipman, **Proc. Natl. Acad. Sci. USA, 85**: 2444 (1988)). The BLAST programs then extend the alignments on the basis of defined match and mismatch criteria.

Motifs which may be detected using the above programs include sequences encoding leucine zippers, helix-turn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

Before searching the cDNAs in the NETGENE™ database for sequence motifs of interest, cDNAs derived from mRNAs which were not of interest were identified and eliminated from further consideration as described in Example 18 below.

EXAMPLE 18

Elimination of Undesired Sequences from Further Consideration

5' ESTs in the NETGENE™ database which were derived from undesired sequences such as transfer RNAs, ribosomal RNAs, mitochondrial RNAs, procaryotic RNAs, fungal RNAs, Alu sequences, L1 sequences, or repeat sequences were identified using the FASTA and BLASTN programs with the parameters listed in Table II.

To eliminate 5' ESTs encoding tRNAs from further consideration, the 5' EST sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. The comparison was performed using FASTA on both strands of the 5' ESTs. Sequences having more than 80% homology over more than 60 nucleotides were identified as tRNA. Of the 144,341 sequences screened, 26 were identified as tRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding rRNAs from further consideration, the 5' EST sequences were compared to the sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as rRNAs. Of the 144,341 sequences screened, 3,312 were identified as rRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding mtRNAs from further consideration, the 5' EST sequences were compared to the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as mtRNAs. Of the 144,341 sequences screened, 6,110 were identified as mtRNAs and eliminated from further consideration.

Sequences which might have resulted from exogenous contaminants were eliminated from further consideration by comparing the 5' EST sequences to release 46 of the EMBL bacterial and fungal divisions using BLASTN with the parameter S=144. All sequences having more than 90% homology over at least 40 nucleotides were identified as exogenous contaminants. Of the 42 cDNA libraries examined, the average percentages of procaryotic and fungal sequences contained therein were 0.2% and 0.5% respectively. Among these sequences, only one could be identified as a sequence specific to fungi. The others were either fungal or procaryotic sequences having homologies with vertebrate sequences or including repeat sequences which had not been masked during the electronic comparison.

In addition, the 5' ESTs were compared to 6093 Alu sequences and 1115 L1 sequences to mask 5' ESTs containing such repeat sequences from further consideration. 5' ESTs including THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats were also eliminated from further consideration. On average, 11.5% of

the sequences in the libraries contained repeat sequences. Of this 11.5%, 7% contained Alu repeats, 3.3% contained L1 repeats and the remaining 1.2% were derived from the other types of repetitive sequences which were screened. These percentages are consistent with those found in cDNA libraries prepared by other groups. For example, the cDNA libraries of Adams et al. contained between 0% and 7.4% Alu repeats depending on the source of the RNA which was used to prepare the cDNA library (Adams et al., *Nature* 377:174, 1996).

The sequences of those 5' ESTs remaining after the elimination of undesirable sequences were compared with the sequences of known human mRNAs to determine the accuracy of the sequencing procedures described above.

EXAMPLE 19

Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described above, the sequences of 5' ESTs derived from known sequences were identified and compared to the known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database. The 6655 5' ESTs which matched a known human mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy.

This analysis revealed that the sequences incorporated in the NETGENE™ database had an accuracy of more than 99.5%.

To determine the efficiency with which the above selection procedures select cDNAs which include the 5' ends of their corresponding mRNAs, the following analysis was performed.

EXAMPLE 20

Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they were derived, the sequences of the ends of the 5' ESTs which were derived from the elongation factor 1 subunit α and ferritin heavy chain genes were compared to the known cDNA sequences for these genes. Since the transcription start sites for the elongation factor 1 subunit α and ferritin heavy chain are well characterized, they may be used to determine the percentage of 5' ESTs derived from these genes which included the authentic transcription start sites.

For both genes, more than 95% of the cDNAs included sequences close to or upstream of the 5' end of the corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the NETGENE™ database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for comparison. For those 5' ESTs derived from mRNAs included in the GeneBank database, more than 85% had their 5' ends close to the 5' ends of the known sequence. As some of the mRNA

sequences available in the GenBank database are deduced from genomic sequences, a 5′ end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5′ ends of their corresponding mRNAs.

The EST libraries made above included multiple 5′ ESTs derived from the same mRNA. The sequences of such 5′ ESTs were compared to one another and the longest 5′ ESTs for each mRNA were identified. Overlapping cDNAs were assembled into continuous sequences (contigs). The resulting continuous sequences were then compared to public databases to gauge their similarity to known sequences, as described in Example 21 below.

EXAMPLE 21

Clustering of the 5′ ESTs and Calculation of Novelty Indices for cDNA Libraries

For each sequenced EST library, the sequences were clustered by the 5′ end. Each sequence in the library was compared to the others with BLASTN2 (direct strand, parameters S = 107). ESTs with High Scoring Segment Pairs (HSPs) at least 25 bp long, having 95% identical bases and beginning closer than 10 bp from each EST 5′ end were grouped. The longest sequence found in the cluster was used as representative of the cluster. A global clustering between libraries was then performed leading to the definition of super-contigs.

To assess the yield of new sequences within the EST libraries, a novelty rate (NR) was defined as: NR = 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating range between 10% and 41% depending on the tissue from which the EST library was obtained. For most of the libraries, the random sequencing of 5′ EST libraries was pursued until the novelty rate reached 20%.

Following characterization as described above, the collection of 5′ ESTs in NETGENE™ was screened to identify those 5′ ESTs bearing potential signal sequences as described in Example 22 below.

EXAMPLE 22

Identification of Potential Signal Sequences in 5′ ESTs

The 5′ ESTs in the NETGENE™ database were screened to identify those having an uninterrupted open reading frame (ORF) longer than 45 nucleotides beginning with an ATG codon and extending to the end of the EST. Approximately half of the cDNA sequences in NETGENE™ contained such an ORF. The ORFs of these 5′ ESTs were searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, G. A New Method for Predicting Signal Sequence Cleavage Sites. **Nucleic Acids Res.** 14:4683-4690 (1986). Those 5′ EST sequences encoding a 15 amino acid long stretch with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those 5′ ESTs which matched a known human mRNA or EST sequence and had a 5′ end more than 20 nucleotides downstream of the known 5′ end were excluded from further analysis. The remaining cDNAs having signal sequences therein were included in a database called SIGNALTAG™.

To confirm the accuracy of the above method for identifying signal sequences, the analysis of Example 23 was performed.

EXAMPLE 23

Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino terminal amino acids of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figures 2 and 3.

Using the above method of identifying secretory proteins, 5' ESTs for human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor all of which are polypeptides which are known to be secreted, were obtained. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide.

To confirm that the signal peptide encoded by the 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs may be cloned into a vector designed for the identification of signal peptides. Some signal peptide identification vectors are designed to confer the ability to grow in selective medium on host cells which have a signal sequence operably inserted into the vector. For example, to confirm that a 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637. Growth of host cells containing signal sequence selection vectors having the signal sequence from the 5' EST inserted therein confirms that the 5' EST encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using the ESTs into expression vectors such as pXT1 (as described below), or by constructing promoter-signal sequence-reporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the medium from cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which encode a functional signal peptide or an authentic secreted protein.

Those 5' ESTs which encoded a signal peptide, as determined by the method of Example 22 above, were further grouped into four categories based on their homology to known sequences. The categorization of the 5' ESTs is described in Example 24 below.

EXAMPLE 24

Categorization of 5' ESTs Encoding a Signal Peptide

Those 5' ESTs having a sequence not matching any known vertebrate sequence nor any publicly available EST sequence were designated "new." Of the sequences in the SIGNALTAG™ database, 947 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs having a sequence not matching any vertebrate sequence but matching a publicly known EST were designated "EST-ext", provided that the known EST sequence was extended by at least 40 nucleotides in the 5' direction. Of the sequences in the SIGNALTAG™ database, 150 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those ESTs not matching any vertebrate sequence but matching a publicly known EST without extending the known EST by at least 40 nucleotides in the 5' direction were designated "EST." Of the sequences in the SIGNALTAG™ database, 599 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs matching a human mRNA sequence but extending the known sequence by at least 40 nucleotides in the 5' direction were designated "VERT-ext." Of the sequences in the SIGNALTAG™ database, 23 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category. Included in this category was a 5' EST which extended the known sequence of the human translocase mRNA by more than 200 bases in the 5' direction. A 5' EST which extended the sequence of a human tumor suppressor gene in the 5' direction was also identified.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Each of the 5' ESTs was categorized based on the tissue from which its corresponding mRNA was obtained, as described below in Example 25.

EXAMPLE 25

Categorization of Expression Patterns

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the above described categories were obtained.

In addition to categorizing the 5' ESTs by the tissue from which the cDNA library in which they were first identified was obtained, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs, as well as their expression levels, may be determined as described in Example 26 below. Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail below.

In addition, 5' ESTs whose corresponding mRNAs are associated with disease states may also be identified. For example, a particular disease may result from lack of expression, over expression, or under expression of an mRNA corresponding to a 5' EST. By comparing mRNA expression patterns and quantities in samples taken from healthy

individuals with those from individuals suffering from a particular disease, 5′ ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5′ ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5′ ESTs. It will also be appreciated that if it is desired to defer characterization until extended cDNAs have been obtained rather than characterizing the ESTs themselves, the above characterization procedures can be applied to characterize the extended cDNAs after their isolation.

EXAMPLE 26

Evaluation of Expression Levels and Patterns of mRNAs Corresponding to 5′ ESTs or Extended cDNAs

Expression levels and patterns of mRNAs corresponding to 5′ ESTs or extended cDNAs (obtainable as described below) may be analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277. Briefly, a 5′ EST, extended cDNA, or fragment thereof corresponding to the gene encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3, T7 or SP6) RNA polymerase promoter to produce antisense RNA. Preferably, the 5′ EST or extended cDNA has 100 or more nucleotides. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (i.e. biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (i.e. RNases CL3, T1, Phy M, U2 or A). The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The 5′ ESTs, extended cDNAs, or fragments thereof may also be tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK Patent Application No. 2 305 241 A. In this method, cDNAs are prepared from a cell, tissue, organism or other source of nucleic acid for which it is desired to determine gene expression patterns. The resulting cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction endonuclease, called an "anchoring enzyme," having a recognition site which is likely to be present at least once in most cDNAs. The fragments which contain the 5′ or 3′ most region of the cleaved cDNA are isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker having a first sequence for hybridization of an amplification primer and an internal restriction site for a "tagging endonuclease" is ligated to the digested cDNAs in the first pool. Digestion with the second endonuclease produces short "tag" fragments from the cDNAs.

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the "tagging endonuclease" to generate short "tag" fragments derived from the cDNAs in the second pool. The "tags" resulting from digestion of the first and second pools with the anchoring enzyme and the tagging endonuclease are ligated to one another to produce "ditags." In some embodiments, the ditags are concatamerized to produce ligation products containing from 2 to 200 ditags. The tag sequences are then determined and compared to the sequences of the 5' ESTs or extended cDNAs to determine which 5' ESTs or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein, the term array means a one dimensional, two dimensional, or multidimensional arrangement of full length cDNAs (i.e. extended cDNAs which include the coding sequence for the signal peptide, the coding sequence for the mature protein, and a stop codon), extended cDNAs, 5' ESTs or fragments of the full length cDNAs, extended cDNAs, or 5' ESTs of sufficient length to permit specific detection of gene expression. Preferably, the fragments are at least 15 nucleotides in length. More preferably, the fragments are at least 100 nucleotides in length. More preferably, the fragments are more than 100 nucleotides in length. In some embodiments the fragments may be more than 500 nucleotides in length.

For example, quantitative analysis of gene expression may be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in a complementary DNA microarray as described by Schena et al. (*Science* 270:467-470, 1995; *Proc. Natl. Acad. Sci. U.S.A.* 93:10614-10619, 1996). Full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are amplified by PCR and arrayed from 96-well microtiter plates onto silylated microscope slides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm^2 microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom filter set. Accurate differential expression measurements are obtained by taking the average of the ratios of two independent hybridizations.

Quantitative analysis of the expression of genes may also be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in complementary DNA arrays as described by Pietu et al. (Genome Research 6:492-503, 1996). The full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides.

After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the 5' ESTs or extended cDNAs can be done through high density nucleotide arrays as described by Lockhart et al. (Nature Biotechnology 14: 1675-1680, 1996) and Sosnowsky et al. (Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of the 5' ESTs or extended cDNAs are synthesized directly on the chip (Lockhart et al., *supra*) or synthesized and then addressed to the chip (Sosnowski et al., *supra*). Preferably, the oligonucleotides are about 20 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are synthesized from the appropriate mRNA population and then randomly fragmented to an average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al., *supra* and application of different electric fields (Sosnowsky et al., Proc. Natl. Acad. Sci. 94:1119-1123)., the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

III. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

Once 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site, the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide. Such extended cDNAs are referred to herein as "full length cDNAs." Alternatively, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

Example 27 below describes a general method for obtaining extended cDNAs. Example 28 below describes the cloning and sequencing of several extended cDNAs, including extended cDNAs which include the entire coding sequence and authentic 5' end of the corresponding mRNA for several secreted proteins.

The methods of Examples 27, 28, and 29 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of the secreted proteins encoded by the genes corresponding to the 5' ESTs. In some embodiments, the extended cDNAs isolated using these methods encode at least 10 amino acids of one of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 20 amino acids of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 30 amino amino acids of the sequences of SEQ ID NOs: 40-140 and

242-377. In a preferred embodiment, the extended cDNAs encode a full length protein sequence, which includes the protein coding sequences of SEQ ID NOs: 40-140 and 242-377.

EXAMPLE 27

General Method for Using 5' ESTs to Clone and Sequence Extended cDNAs

The following general method has been used to quickly and efficiently isolate extended cDNAs including sequence adjacent to the sequences of the 5' ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST in the NETGENE™ database, including those 5' ESTs encoding secreted proteins. The method is summarized in Figure 6.

1. Obtaining Extended cDNAs

a) First strand synthesis

The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly 14dT primer containing a 49 nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. For example, the primer may have the following sequence: 5'-ATC GTT GAG ACT CGT ACC AGC AGA GTC ACG AGA GAG ACT ACA CGG TAC TGG TTT TTT TTT TTT TTVN -3' (SEQ ID NO:14). Those skilled in the art will appreciate that other sequences may also be added to the poly dT sequence and used to prime the first strand synthesis. Using this primer and a reverse transcriptase such as the Superscript II (Gibco BRL) or Rnase H Minus M-MLV (Promega) enzyme, a reverse transcript anchored at the 3' polyA site of the RNAs is generated.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer are eliminated with an exclusion column such as an AcA34 (Biosepra) matrix as explained in Example 11.

b) Second strand synthesis

A pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Software used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, *PCR Meth. Appl.* **1**:124-128, 1991), or based on the octamer frequency disparity method (Griffais et al., *Nucleic Acids Res.* **19**: 3887-3891, 1991 such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html).

Preferably, the nested primers at the 5' end are separated from one another by four to nine bases. The 5' primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

Preferably, the nested primers at the 3' end are separated from one another by four to nine bases. For example, the nested 3' primers may have the following sequences: (5'- CCA GCA GAG TCA CGA GAG AGA CTA CAC GG -3'(SEQ ID NO:15), and 5'- CAC GAG AGA GAC TAC ACG GTA CTG G -3' (SEQ ID NO:16). These primers were selected because they have melting temperatures and specificities compatible with their use in PCR. However, those skilled in the art will appreciate that other sequences may also be used as primers.

The first PCR run of 25 cycles is performed using the Advantage Tth Polymerase Mix (Clontech) and the outer primer from each of the nested pairs. A second 20 cycle PCR using the same enzyme and the inner primer from each of the nested pairs is then performed on 1/2500 of the first PCR product. Thereafter, the primers and nucleotides are removed.

2. Sequencing of Full Length Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the OSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the whole coding sequence. Such a full length extended cDNA undergoes a direct cloning procedure as described in section a below. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b below.

a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST sequence, it is cloned in an appropriate vector such as pED6dpc2, as described in section 3.

b) Nested PCR products containing incomplete ORFs

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products as described in the following section.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, i.e. the polyA tract and sometimes the polyadenylation signal, as illustrated in figure 6. Such full length extended cDNAs are then cloned into an appropriate vector as described in section 3.

c) Sequencing extended cDNAs

Sequencing of extended cDNAs is performed using a Die Terminator approach with the AmpliTaq DNA polymerase FS kit available from Perkin Elmer.

In order to sequence PCR fragments, primer walking is performed using software such as OSP to choose primers and automated computer software such as ASMG (Sutton et al., *Genome Science Technol.* **1**: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag using minimum overlaps of 32 nucleotides. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment is assessed as follows. Since sequences located after a polyA tract are difficult to determine precisely in the case of uncloned products, sequencing and primer

walking processes for PCR products are interrupted when a polyA tract is identified in extended cDNAs obtained as described in case b. The sequence length is compared to the size of the nested PCR product obtained as described above. Due to the limited accuracy of the determination of the PCR product size by gel electrophoresis, a sequence is considered complete if the size of the obtained sequence is at least 70 % the size of the first nested PCR product. If the length of the sequence determined from the computer analysis is not at least 70% of the length of the nested PCR product, these PCR products are cloned and the sequence of the insertion is determined. When Northern blot data are available, the size of the mRNA detected for a given PCR product is used to finally assess that the sequence is complete. Sequences which do not fulfill the above criteria are discarded and will undergo a new isolation procedure.

Sequence data of all extended cDNAs are then transferred to a proprietary database, where quality controls and validation steps are carried out as described in example 15.

3. <u>Cloning of Full Length Extended cDNAs</u>

The PCR product containing the full coding sequence is then cloned in an appropriate vector. For example, the extended cDNAs can be cloned into the expression vector pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA) as follows. The structure of pED6dpc2 is shown in Figure 7. pED6dpc2 vector DNA is prepared with blunt ends by performing an EcoRI digestion followed by a fill in reaction. The blunt ended vector is dephosphorylated. After removal of PCR primers and ethanol precipitation, the PCR product containing the full coding sequence or the extended cDNA obtained as described above is phosphorylated with a kinase subsequently removed by phenol-Sevag extraction and precipitation. The double stranded extended cDNA is then ligated to the vector and the resulting expression plasmid introduced into appropriate host cells.

Since the PCR products obtained as described above are blunt ended molecules that can be cloned in either direction, the orientation of several clones for each PCR product is determined. Then, 4 to 10 clones are ordered in microtiter plates and subjected to a PCR reaction using a first primer located in the vector close to the cloning site and a second primer located in the portion of the extended cDNA corresponding to the 3' end of the mRNA. This second primer may be the antisense primer used in anchored PCR in the case of direct cloning (case a) or the antisense primer located inside the 3'UTR in the case of indirect cloning (case b). Clones in which the start codon of the extended cDNA is operably linked to the promoter in the vector so as to permit expression of the protein encoded by the extended cDNA are conserved and sequenced. In addition to the ends of cDNA inserts, approximately 50 bp of vector DNA on each side of the cDNA insert are also sequenced.

The cloned PCR products are then entirely sequenced according to the aforementioned procedure. In this case, contig assembly of long fragments is then performed on walking sequences that have already contigated for uncloned PCR products during primer walking. Sequencing of cloned amplicons is complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends.

4. <u>Computer Analysis of Full Length Extended cDNA</u>

Sequences of all full length extended cDNAs are then submitted to further analysis as described below and using the parameters found in Table II with the following modifications. For screening of miscellaneous subdivisions of Genbank, FASTA was used instead of BLASTN and 15 nucleotide of homology was the limit instead of 17. For Alu detection, BLASTN was used with the following parameters: S = 72; identity = 70%; and length = 40 nucleotides. Polyadenylation signal and polyA tail which were not search for the 5' ESTs were searched. For polyadenylation signal detection the signal (AATAAA) was searched with one permissible mismatch in the last ten nucleotides preceding the 5' end of the polyA. For the polyA, a stretch of 8 amino acids in the last 20 nucleotides of the sequence was searched with BLAST2N in the sense strand with the following parameters (W = 6, S = 10, E = 1000, and identity = 90%). Finally, patented sequences and ORF homologies were searched using, respectively, BLASTN and BLASTP on GenSEQ (Derwent's database of patented nucleotide sequences) and SWISSPROT for ORFs with the following parameters (W = 8 and B = 10). Before examining the extended full length cDNAs for sequences of interest, extended cDNAs which are not of interest are searched as follows.

a) Elimination of undesired sequences

Although 5'ESTs were checked to remove contaminant sequences as described in Example 18, a last verification was carried out to identify extended cDNAs sequences derived from undesired sequences such as vector RNAs, transfer RNAs, ribosomal rRNAs, mitochondrial RNAs, prokaryotic RNAs and fungal RNAs using the FASTA and BLASTN programs on both strands of extended cDNAs as described below.

To identify the extended cDNAs encoding vector RNAs, extended cDNAs are compared to the known sequences of vector RNA using the FASTA program. Sequences of extended cDNAs with more than 90% homology over stretches of 15 nucleotides are identified as vector RNA.

To identify the extended cDNAs encoding tRNAs, extended cDNA sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. Sequences of extended cDNAs having more than 80% homology over 60 nucleotides using FASTA were identified as tRNA.

To identify the extended cDNAs encoding rRNAs, extended cDNA sequences were compared to the sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. Sequences of extended cDNAs having more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as rRNAs.

To identify the extended cDNAs encoding mtRNAs, extended cDNA sequences were compared to the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. Sequences of extended cDNAs having more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as mtRNAs.

Sequences which might have resulted from other exogenous contaminants were identified by comparing extended cDNA sequences to release 105 of Genbank bacterial and fungal divisions. Sequences of extended cDNAs

having more than 90% homology over 40 nucleotides using BLASTN were identified as exogenous prokaryotic or fungal contaminants.

In addition, extended cDNAs were searched for different repeat sequences, including Alu sequences, L1 sequences, THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats. Sequences of extended cDNAs with more than 70% homology over 40 nucleotide stretches using BLASTN were identified as repeat sequences and masked in further identification procedures. In addition, clones showing extensive homology to repeats, i.e., matches of either more than 50 nucleotides if the homology was at least 75% or more than 40 nucleotides if the homology was at least 85% or more than 30 nucleotides if the homology was at least 90%, were flagged.

b) Identification of structural features

Structural features, e.g. polyA tail and polyadenylation signal, of the sequences of full length extended cDNAs are subsequently determined as follows.

A polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it. The polyA tail search is restricted to the last 20 nt of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not readable after such a polyA stretch. Stretches with 100% homology over 6 nucleotides are identified as polyA tails.

To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 bp preceding the polyA tail are searched for the canonic polyadenylation AAUAAA signal allowing one mismatch to account for possible sequencing errors and known variation in the canonical sequence of the polyadenylation signal.

c) Identification of functional features

Functional features, e.g. ORFs and signal sequences, of the sequences of full length extended cDNAs were subsequently determined as follows.

The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation initiation codon and ending with a stop codon. ORFs encoding at least 20 amino acids are preferred.

Each found ORF is then scanned for the presence of a signal peptide in the first 50 amino-acids or, where appropriate, within shorter regions down to 20 amino acids or less in the ORF, using the matrix method of von Heijne (Nuc. Acids Res. 14: 4683-4690 (1986)) and the modification described in Example 22.

d) Homology to either nucleotidic or proteic sequences

Sequences of full length extended cDNAs are then compared to known sequences on a nucleotidic or proteic basis.

Sequences of full length extended cDNAs are compared to the following known nucleic acid sequences: vertebrate sequences (Genbank), EST sequences (Genbank), patented sequences (Geneseqn) and recently identified sequences (Genbank daily releases) available at the time of filing for the priority documents. Full length cDNA sequences are also compared to the sequences of a private database (Genset internal sequences) in order to find sequences that

have already been identified by applicants. Sequences of full length extended cDNAs with more than 90% homology over 30 nucleotides using either BLASTN or BLAST2N as indicated in Table III are identified as sequences that have already been described. Matching vertebrate sequences are subsequently examined using FASTA; full length extended cDNAs with more than 70% homology over 30 nucleotides are identified as sequences that have already been described.

ORFs encoded by full length extended cDNAs as defined in section c) are subsequently compared to known amino acid sequences found in Swissprot release CHP, PIR release PIR# and Genpept release GPEPT public databases using BLASTP with the parameter W=8 and allowing a maximum of 10 matches. Sequences of full length extended cDNAs showing extensive homology to known protein sequences are recognized as already identified proteins.

In addition, the three-frame conceptual translation products of the top strand of full length extended cDNAs are compared to publicly known amino acid sequences of Swissprot using BLASTX with the parameter E=0.001. Sequences of full length extended cDNAs with more than 70% homology over 30 amino acid stretches are detected as already identified proteins.

5. Selection of Cloned Full Length Sequences of the Present Invention

Cloned full length extended cDNA sequences that have already been characterized by the aforementioned computer analysis are then submitted to an automatic procedure in order to preselect full length extended cDNAs containing sequences of interest.

a) Automatic sequence preselection

All complete cloned full length extended cDNAs clipped for vector on both ends are considered. First, a negative selection is operated in order to eliminate unwanted cloned sequences resulting from either contaminants or PCR artifacts as follows. Sequences matching contaminant sequences such as vector RNA, tRNA, mtRNA, rRNA sequences are discarded as well as those encoding ORF sequences exhibiting extensive homology to repeats as defined in section 4 a). Sequences obtained by direct cloning using nested primers on 5' and 3' tags (section 1. case a) but lacking polyA tail are discarded. Only ORFs containing a signal peptide and ending either before the polyA tail (case a) or before the end of the cloned 3'UTR (case b) are kept. Then, ORFs containing unlikely mature proteins such as mature proteins which size is less than 20 amino acids or less than 25% of the immature protein size are eliminated.

In the selection of the OFR, priority was given to the ORF and the frame corresponding to the polypeptides described in SignalTag Patents (United States Patent Application Serial Nos: 08/905,223; 08/905,135; 08/905,051; 08/905,144; 08/905,279; 08/904,468; 08/905,134; and 08/905,133). If the ORF was not found among the OFRs described in the SignalTag Patents, the ORF encoding the signal peptide with the highest score according to Von Heijne method as defined in Example 22 was chosen. If the scores were identical, then the longest ORF was chosen.

Sequences of full length extended cDNA clones are then compared pairwise with BLAST after masking of the repeat sequences. Sequences containing at least 90% homology over 30 nucleotides are clustered in the same class. Each cluster is then subjected to a cluster analysis that detects sequences resulting from internal priming or from

alternative splicing, identical sequences or sequences with several frameshifts. This automatic analysis serves as a basis for manual selection of the sequences.

b) Manual sequence selection

Manual selection is carried out using automatically generated reports for each sequenced full length extended cDNA clone. During this manual procedures, a selection is operated between clones belonging to the same class as follows. ORF sequences encoded by clones belonging to the same class are aligned and compared. If the homology between nucleotidic sequences of clones belonging to the same class is more than 90% over 30 nucleotide stretches or if the homology between amino acid sequences of clones belonging to the same class is more than 80% over 20 amino acid stretches, than the clones are considered as being identical. The chosen ORF is the best one according to the criteria mentioned below. If the nucleotide and amino acid homologies are less than 90% and 80% respectively, the clones are said to encode distinct proteins which can be both selected if they contain sequences of interest.

Selection of full length extended cDNA clones encoding sequences of interest is performed using the following criteria. Structural parameters (initial tag, polyadenylation site and signal) are first checked. Then, homologies with known nucleic acids and proteins are examined in order to determine whether the clone sequence match a known nucleic/proteic sequence and, in the latter case, its covering rate and the date at which the sequence became public. If there is no extensive match with sequences other than ESTs or genomic DNA, or if the clone sequence brings substantial new information, such as encoding a protein resulting from alternative slicing of an mRNA coding for an already known protein, the sequence is kept. Examples of such cloned full length extended cDNAs containing sequences of interest are described in Example 28. Sequences resulting from chimera or double inserts as assessed by homology to other sequences are discarded during this procedure.

EXAMPLE 28

Cloning and Sequencing of Extended cDNAs

The procedure described in Example 27 above was used to obtain the extended cDNAs of the present invention. Using this approach, the full length cDNA of SEQ ID NO:17 was obtained. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 18) having a von Heijne score of 8.2.

The full length cDNA of SEQ ID NO:19 was also obtained using this procedure. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:20) having a von Heijne score of 5.5.

Another full length cDNA obtained using the procedure described above has the sequence of SEQ ID NO:21. This cDNA, falls into the "EST-ext" category described above and encodes the signal peptide MVLTTLPSANSANSPVNMPTTGPNSLSYASSALSPCLT (SEQ ID NO:22) having a von Heijne score of 5.9.

The above procedure was also used to obtain a full length cDNA having the sequence of SEQ ID NO:23. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide ILSTVTALTFAXA (SEQ ID NO:24) having a von Heijne score of 5.5.

The full length cDNA of SEQ ID NO:25 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LVLTLCTLPLAVA (SEQ ID NO:26) having a von Heijne score of 10.1.

The full length cDNA of SEQ ID NO:27 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:28) having a von Heijne score of 10.7.

The above procedures were also used to obtain the extended cDNAs of the present invention. 5' ESTs expressed in a variety of tissues were obtained as described above. The appended sequence listing provides the tissues from which the extended cDNAs were obtained. It will be appreciated that the extended cDNAs may also be expressed in tissues other than the tissue listed in the sequence listing.

5' ESTs obtained as described above were used to obtain extended cDNAs having the sequences of SEQ ID NOs: 40-140 and 242-377. Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEQ ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading Poly A Signal Location in Table IV) and the locations of polyA sites (listed under the heading Poly A Site Location in Table IV).

The polypeptides encoded by the extended cDNAs were screened for the presence of known structural or functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the members of a protein family. The conserved regions have been used to derive consensus patterns or matrices included in the PROSITE data bank, in particular in the file prosite.dat (Release 13.0 of November 1995, located at http://expasy.hcuge.ch/sprot/prosite.html. Prosite_convert and prosite_scan programs (http://ulrec3.unil.ch/ftpserveur/prosite_scan) were used to find signatures on the extended cDNAs.

For each pattern obtained with the prosite_convert program from the prosite.dat file, the accuracy of the detection on a new protein sequence has been tested by evaluating the frequency of irrelevant hits on the population of human secreted proteins included in the data bank SWISSPROT. The ratio between the number of hits on shuffled proteins (with a window size of 20 amino acids) and the number of hits on native (unshuffled) proteins was used as an index. Every pattern for which the ration was greater than 20% (one hit on shuffled proteins for 5 hits on native

proteins) was skipped during the search with prosite_scan. The program used to shuffle protein sequences (db_shuffled) and the program used to determine the statistics for each pattern in the protein data banks (prosite_statistics) are available on the ftp site http://ulrec3.unil.ch/ftpserveur/prosite_scan.

Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the mature polypeptide created by cleaving the signal peptide from the full length polypeptide (fourth column).

The nucleotide sequences of the sequences of SEQ ID NOs: 40-140 and 242-377 and the amino acid sequences encoded by SEQ ID NOs: 40-140 and 242-377 (i.e. amino acid sequences of SEQ ID NOs: 141-241 and 378-513) are provided in the appended sequence listing. In some instances, the sequences are preliminary and may include some incorrect or ambiguous sequences or amino acids. The sequences of SEQ ID NOs: 40-140 and 242-377 can readily be screened for any errors therein and any sequence ambiguities can be resolved by resequencing a fragment containing such errors or ambiguities on both strands. Nucleic acid fragments for resolving sequencing errors or ambiguities may be obtained from the deposited clones or can be isolated using the techniques described herein. Resolution of any such ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences encoded by the DNA containing the error or ambiguity. For example, in the sequences of the present invention, ambiguities in the sequence of SEQ ID NO: 131 were resolved. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein, and determining its sequence.

For each amino acid sequence, Applicants have identified what they have determined to be the reading frame best identifiable with sequence information available at the time of filing. Some of the amino acid sequences may contain "Xaa" designators. These "Xaa" designators indicate either (1) a residue which cannot be identified because of nucleotide sequence ambiguity or (2) a stop codon in the determined sequence where Applicants believe one should not exist (if the sequence were determined more accurately).

Cells containing the extended cDNAs (SEQ ID NOs: 40-140 and 242-377) of the present invention in the vector pED6dpc2, are maintained in permanent deposit by the inventors at Genset, S.A., 24 Rue Royale, 75008 Paris, France.

Pools of cells containing the extended cDNAs (SEQ ID NOs: 40-140 and 242-377), from which cells containing a particular polynucleotide are obtainable, were deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209 or the European Collection of Cell Cultures, Vaccine Research and Production Laboratory, Public Health Laboratory Service, Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom. Each extended cDNA clone has been transfected into separate bacterial cells (E-

coli) for this composite deposit. Table VI lists the deposit numbers of the clones containing the extended cDNAs of the present invention. Table VII provides the internal designation number assigned to each SEQ ID NO and indicates whether the sequence is a nucleic acid sequence or a protein sequence.

Each extended cDNA can be removed from the pED6dpc2 vector in which it was deposited by performing a NotI, PstI double digestion to produce the appropriate fragment for each clone. The proteins encoded by the extended cDNAs may also be expressed from the promoter in pED6dpc2.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The design of the oligonucleotide probe should preferably follow these parameters:

(a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;

(b) Preferably, the probe is designed to have a T_m of approx. 80°C (assuming 2 degrees for each A or T and 4 degrees for each G or C). However, probes having melting temperatures between 40 °C and 80 °C may also be used provided that specificity is not lost.

The oligonucleotide should preferably be labeled with (-[^{32}P]ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantified by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately $4X10^6$ dpm/pmole.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 µl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 ug/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 µg/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaC1/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 pg/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to $1X10^6$ dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to

1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the extended cDNA insertion. For example, a PCR reaction may be conducted using a primer having the sequence GGCCATACACTTGAGTGAC (SEQ ID NO:38) and a primer having the sequence ATATAGACAAACGCACACC (SEQ. ID. NO:39). The PCR product which corresponds to the extended cDNA can then be manipulated using standard cloning techniques familiar to those skilled in the art.

In addition to PCR based methods for obtaining extended cDNAs, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs or 5' ESTs. Example 29 below provides an example of such methods.

EXAMPLE 29

Methods for Obtaining Extended cDNAs or Nucleic Acids Homologous to Extended cDNAs or 5' ESTs

A full length cDNA library can be made using the strategies described in Examples 13, 14, 15, and 16 above by replacing the random nonamer used in Example 14 with an oligo-dT primer. For instance, the oligonucleotide of SEQ ID NO:14 may be used.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art. The library includes cDNAs which are derived from the mRNA corresponding to a 5' EST or which have homology to an extended cDNA or 5' EST. The cDNA library or genomic DNA library is hybridized to a detectable probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA using conventional techniques. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 30 nucleotides from the 5' EST or extended cDNA. In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. A probe comprising at least 10 consecutive nucleotides from the 5' EST or extended

cDNA is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, in vitro transcription, and non-radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter and denatured. After incubation of the filter with a blocking solution, the filter is contacted with the labeled probe and incubated for a sufficient amount of time for the probe to hybridize to cDNAs or genomic DNAs containing a sequence capable of hybridizing to the probe.

By varying the stringency of the hybridization conditions used to identify extended cDNAs or genomic DNAs which hybridize to the detectable probe, extended cDNAS having different levels of homology to the probe can be identified and isolated. To identify extended cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: $Tm = 81.5 + 16.6(\log [Na+]) + 0.41(\text{fraction } G+C) - (600/N)$ where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation $Tm = 81.5 + 16.6(\log [Na+]) + 0.41(\text{fraction } G+C) - (0.63\% \text{ formamide}) - (600/N)$ where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100μg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100μg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook et al., supra.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions. Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed

with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Extended cDNAs, nucleic acids homologous to extended cDNAs or 5' ESTs, or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

The above procedure may be modified to identify extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a $Na+$ concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide.

Extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs which have hybridized to the probe are identified by autoradiography.

If it is desired to obtain nucleic acids homologous to extended cDNAs, such as allelic variants thereof or nucleic acids encoding proteins related to the proteins encoded by the extended cDNAs, the level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may readily be determined. To determine the level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived are compared. For example, using the above methods, nucleic acids having at least 95% nucleic acid homology to the extended cDNA or 5'EST from which the probe was derived may be obtained and identified. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA or 5'EST from which the probe was derived. The level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may be further determined using BLAST2N; parameters may be adapted depending on the sequence length and degree of homology studied. In such comparisons, the default parameters or the parameters listed in Tables II and III may be used.

To determine whether a clone encodes a protein having a given amount of homology to the protein encoded by the extended cDNA or 5' EST, the amino acid sequence encoded by the extended cDNA or 5' EST is compared to the amino acid sequence encoded by the hybridizing nucleic acid. Homology is determined to exist when an amino acid sequence in the extended cDNA or 5' EST is closely related to an amino acid sequence in the hybridizing nucleic acid. A

sequence is closely related when it is identical to that of the extended cDNA or 5' EST or when it contains one or more amino acid substitutions therein in which amino acids having similar characteristics have been substituted for one another. Using the above methods, one can obtain nucleic acids encoding proteins having at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the proteins encoded by the extended cDNA or 5'EST from which the probe was derived. Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied the level of homology may be determined. In determining the level of homology using FASTA, the default parameters or the parameters listed in Tables II or III may be used.

Alternatively, extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing poly A selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the poly A tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of the 5' EST for which an extended cDNA is desired. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the sequences of the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the sequences of the 5' EST. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of the 5' EST. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RTPCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by contacting an mRNA comprising the sequence of the 5' EST for which an extended cDNA is desired with a primer comprising at least 10 consecutive nucleotides of the sequences complementary to the 5' EST, hybridizing the primer to the mRNAs, and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the 5' EST.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, avian, or insect cell.

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double

stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al. Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989.

Alternatively, kits for obtaining full length cDNAs, such as the GeneTrapper (Cat. No. 10356-020, Gibco, BRL), may be used for obtaining full length cDNAs or extended cDNAs. In this approach, full length or extended cDNAs are prepared from mRNA and cloned into double stranded phagemids. The cDNA library in the double stranded phagemids is then rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1, and Exonuclease III as described in the manual accompanying the GeneTrapper kit. A biotinylated oligonucleotide comprising the sequence of a 5' EST, or a fragment containing at least 10 nucleotides thereof, is hybridized to the single stranded phagemids. Preferably, the fragment comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the fragment comprises 20-30 consecutive nucleotides from the 5' EST. In some procedures, the fragment may comprise more than 30 consecutive nucleotides from the 5' EST. For example, the fragment may comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST.

Hybrids between the biotinylated oligonucleotide and phagemids having inserts containing the 5' EST sequence are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet. Thereafter, the resulting phagemids containing the 5' EST sequence are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST sequence. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs containing the 5' EST sequence are identified by colony PCR or colony hybridization.

A plurality of extended cDNAs containing full length protein coding sequences or sequences encoding only the mature protein remaining after the signal peptide is cleaved may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

IV. Expression of Proteins Encoded by Extended cDNAs Isolated Using 5' ESTs

Extended cDNAs containing the full protein coding sequences of their corresponding mRNAs or portions thereof, such as cDNAs encoding the mature protein, may be used to express the secreted proteins or portions thereof which they encode as described in Example 30 below. If desired, the extended cDNAs may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. It will be appreciated that a plurality of extended cDNAs containing the full protein coding sequences or portions thereof may be simultaneously cloned into expression vectors to create an expression library for analysis of the encoded proteins as described below.

EXAMPLE 30

Expression of the Proteins Encoded by Extended cDNAs or Portions Thereof

To express the proteins encoded by the extended cDNAs or portions thereof, nucleic acids containing the coding sequence for the proteins or portions thereof to be expressed are obtained as described in Examples 27-29 and cloned into a suitable expression vector. If desired, the nucleic acids may contain the sequences encoding the signal

peptide to facilitate secretion of the expressed protein. For example, the nucleic acid may comprise the sequence of one of SEQ ID NOs: 40-140 and 242-377 listed in Table IV and in the accompanying sequence listing. Alternatively, the nucleic acid may comprise those nucleotides which make up the full coding sequence of one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the full coding sequence (i.e. the sequence encoding the signal peptide and the mature protein resulting from cleavage of the signal peptide) differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the full coding sequences in the sequences of SEQ ID NOs. 40-140 and 242-377. For example, the sequence of SEQ ID NO: 115 represents an alternatively spliced transcript of a previously identified mRNA.. Accordingly, the scope of any claims herein relating to nucleic acids containing the full coding sequence of one of SEQ ID NOs. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the full coding sequences listed in Table IV Similarly, should the extent of the full length polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the amino acid sequence of the full length polypeptides is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V.

Alternatively, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the mature protein (i.e. the protein created by cleaving the signal peptide off) encoded by one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the sequence encoding the mature protein differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the mature protein in the sequences of SEQ ID NOs. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids containing the sequence encoding the mature protein encoded by one of SEQ ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table IV. Thus, claims relating to nucleic acids containing the sequence encoding the mature protein encompass equivalents to the sequences listed in Table IV, such as sequences encoding biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in addition to cleavage of the signal peptide. Similarly, should the extent of the mature polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a mature protein included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V. Thus, claims relating to polypeptides comprising the sequence of the mature protein encompass equivalents to the sequences

listed in Table IV, such as biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in addition to cleavage of the signal peptide. It will also be appreciated that should the biologically active form of the polypeptides included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 or the nucleic acids encoding the biologically active form of the polypeptides differ from those identified as the mature polypeptide in Table V or the nucleotides encoding the mature polypeptide in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the amino acids in the biologically active form of the polypeptides and the nucleic acids encoding the biologically active form of the polypeptides. In such instances, the claims relating to polypetides comprising the mature protein included in one of SEQ ID NOs. 141-241 and 378-513 or nucleic acids comprising the nucleotides of one of SEQ ID NOs. 40-140 and 242-377 encoding the mature protein shall not be construed to exclude any readily identifiable variations from the sequences listed in Table IV and Table V.

In some embodiments, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the signal peptide encoded by one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the sequence encoding the signal peptide differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the signal peptide in the sequences of SEQ ID NOs. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids containing the sequence encoding the signal peptide encoded by one of SEQ ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table IV. Similarly, should the extent of the signal peptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a signal peptide included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table V.

Alternatively, the nucleic acid may encode a polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the nucleic acid may encode a polypeptide comprising at least 15 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 60, at least 75, at least 100 or more than 100 consecutive amino acids of one of the sequences of SEQ ID Nos: 141-241 and 378-513.

The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767.

The following is provided as one exemplary method to express the proteins encoded by the extended cDNAs corresponding to the 5' ESTs or the nucleic acids described above. First, the methionine initiation codon for the gene and the poly A signal of the gene are identified. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the extended cDNA lacks a poly A signal, this sequence can be added to the construct by, for example, splicing out the Poly A signal from pSG5 (Stratagene) using BglI and SalI restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the *gag* gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex Thymidine Kinase promoter and the selectable neomycin gene. The extended cDNA or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the extended cDNA or portion thereof and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and BglII at the 5' end of the corresponding cDNA 3' primer, taking care to ensure that the extended cDNA is positioned in frame with the poly A signal. The purified fragment obtained from the resulting PCR reaction is digested with PstI, blunt ended with an exonuclease, digested with Bgl II, purified and ligated to pXT1, now containing a poly A signal and digested with BglII.

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600ug/ml G418 (Sigma, St. Louis, Missouri). Preferably the expressed protein is released into the culture medium, thereby facilitating purification.

Alternatively, the extended cDNAs may be cloned into pED6dpc2 as described above. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. Preferably, the protein expressed from the extended cDNA is released into the culture medium thereby facilitating purification.

Proteins in the culture medium are separated by gel electrophoresis. If desired, the proteins may be ammonium sulfate precipitated or separated based on size or charge prior to electrophoresis.

As a control, the expression vector lacking a cDNA insert is introduced into host cells or organisms and the proteins in the medium are harvested. The secreted proteins present in the medium are detected using techniques such as Coomassie or silver staining or using antibodies against the protein encoded by the extended cDNA. Coomassie and silver staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate 5' EST, extended cDNA, or portion thereof. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the 5' EST, extended cDNA, or portion thereof.

Secreted proteins from the host cells or organisms containing an expression vector which contains the extended cDNA derived from a 5' EST or a portion thereof are compared to those from the control cells or organism. The presence of a band in the medium from the cells containing the expression vector which is absent in the medium from the control cells indicates that the extended cDNA encodes a secreted protein. Generally, the band corresponding to the protein encoded by the extended cDNA will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector containing an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

The protein encoded by the extended cDNA may be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques.

If antibody production is not possible, the extended cDNA sequence or portion thereof may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the extended cDNA or portion thereof is inserted in frame with the gene encoding the other half of

the chimera. The other half of the chimera may be β-globin or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to β-globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the β-globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β-globin chimerics is pSG5 (Stratagene), which encodes rabbit β-globin. Intron II of the rabbit β-globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis et al., (**Basic Methods in Molecular Biology**, L.G. Davis, M.D. Dibner, and J.F. Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may additionally be produced from the construct using in vitro translation systems such as the In vitro Express™ Translation Kit (Stratagene).

Following expression and purification of the secreted proteins encoded by the 5′ ESTs, extended cDNAs, or fragments thereof, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 31 below. It will be appreciated that a plurality of proteins expressed from these cDNAs may be included in a panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

EXAMPLE 31

Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

The proteins encoded by the 5′ ESTs, extended cDNAs, or fragments thereof are cloned into expression vectors such as those described in Example 30. The proteins are purified by size, charge, immunochromatography or other techniques familiar to those skilled in the art. Following purification, the proteins are labeled using techniques known to those skilled in the art. The labeled proteins are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are washed to remove non-specifically bound protein. The labeled proteins are detected by autoradiography. Alternatively, unlabeled proteins may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

Specificity of cell surface binding may be analyzed by conducting a competition analysis in which various amounts of unlabeled protein are incubated along with the labeled protein. The amount of labeled protein bound to the cell surface decreases as the amount of competitive unlabeled protein increases. As a control, various amounts of an unlabeled protein unrelated to the labeled protein is included in some binding reactions. The amount of labeled protein bound to the cell surface does not decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein encoded by the cDNA binds specifically to the cell surface.

As discussed above, secreted proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The secreted proteins encoded by the extended cDNAs or portions thereof made according to Examples 27-29 may be evaluated to determine their physiological activities as described below.

EXAMPLE 32

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Cytokine, Cell Proliferation or Cell Differentiation Activity

As discussed above, secreted proteins may act as cytokines or may affect cellular proliferation or differentiation. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7c and CMK. The proteins encoded by the above extended cDNAs or portions thereof may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references: **Current Protocols in Immunology**, Ed. by J.E. Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. **J. Immunol.** 137:3494-3500, 1986. Bertagnolli et al. **J. Immunol.** 145:1706-1712, 1990. Bertagnolli et al., **Cellular Immunology** 133:327-341, 1991. Bertagnolli, et al. **J. Immunol.** 149:3778-3783, 1992; Bowman et al., **J. Immunol.** 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells and thymocytes are known. These include the techniques disclosed in **Current Protocols in Immunology**. J.E. Coligan et al. Eds., Vol 1 pp. 3.12.1-3.12.14 John Wiley and Sons, Toronto. 1994; and Schreiber, R.D. **Current Protocols in Immunology**., *supra* Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references: Bottomly, K., Davis, L.S. and Lipsky, P.E., Measurement of Human and Murine Interleukin 2 and Interleukin 4, **Current Protocols in Immunology**., J.E. Coligan et al. Eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., **J. Exp. Med.** 173:1205-1211, 1991; Moreau et al., **Nature** 36:690-692, 1988; Greenberger et al., **Proc. Natl. Acad. Sci. U.S.A.** 80:2931-2938, 1983; Nordan, R., Measurement of Mouse and Human Interleukin 6 **Current Protocols in Immunology**. J.E. Coligan et al. Eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., **Proc. Natl. Acad. Sci. U.S.A.** 83:1857-1861, 1986; Bennett, F., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Human Interleukin 11 **Current Protocols in Immunology**. J.E. Coligan et al. Eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Mouse and Human Interleukin 9 **Current Protocols in Immunology**. J.E. Coligan et al., Eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

The proteins encoded by the cDNAs may also be assayed for their ability to regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in **Current Protocols in Immunology**, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Weinberger et al., **Proc. Natl. Acad. Sci. USA** 77:6091-6095, 1980; Weinberger et al., **Eur. J. Immun.** 11:405-411, 1981; Takai et al., **J. Immunol.** 137:3494-3500, 1986; Takai et al., **J. Immunol.** 140:508-512, 1988.

Those proteins which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 33

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Activity as Immune System Regulators

The proteins encoded by the cDNAs may also be evaluated for their effects as immune regulators. For example, the proteins may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in **Current Protocols in Immunology**, J.E. Coligan et al. Eds, Greene Publishing Associates and Wiley-Interscience; Herrmann et al., **Proc. Natl. Acad. Sci. USA** 78:2488-2492, 1981; Herrmann et al., **J. Immunol.** 128:1968-1974, 1982; Handa et al., **J. Immunol.** 135:1564-1572, 1985; Takai et al., **J. Immunol.** 137:3494-3500, 1986; Takai et al., **J. Immunol.** 140:508-512, 1988; Herrmann et al., **Proc. Natl. Acad. Sci. USA** 78:2488-2492, 1981; Herrmann et al., **J. Immunol.** 128:1968-1974, 1982; Handa et al., **J. Immunol.** 135:1564-1572, 1985; Takai et al., **J. Immunol.** 137:3494-3500, 1986; Bowman et al., **J. Virology** 61:1992-1998; Takai et al., **J. Immunol.** 140:508-512, 1988; Bertagnolli et al., **Cellular Immunology** 133:327-341, 1991; Brown et al., **J. Immunol.** 153:3079-3092, 1994.

The proteins encoded by the cDNAs may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Maliszewski, **J. Immunol.** 144:3028-3033, 1990; Mond, J.J. and Brunswick, M Assays for B Cell Function: *In vitro* Antibody Production, Vol 1 pp. 3.8.1-3.8.16 in **Current Protocols in Immunology**. J.E. Coligan et al Eds., John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte

Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in **Current Protocols in Immunology**, J.E. Coligan et al. Eds., Greene Publishing Associates and Wiley-Interscience; Takai et al., **J. Immunol.** 137:3494-3500, 1986; Takai et al.; **J. Immunol.** 140:508-512, 1988; Bertagnolli et al., **J. Immunol.** 149:3778-3783, 1992.

The proteins encoded by the cDNAs may also be evaluated for their effect on dendritic cell mediated activation of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Guery et al., **J. Immunol.** 134:536-544, 1995; Inaba et al., **Journal of Experimental Medicine** 173:549-559, 1991; Macatonia et al., **Journal of Immunology** 154:5071-5079, 1995; Porgador et al., **Journal of Experimental Medicine** 182:255-260, 1995; Nair et al., **Journal of Virology** 67:4062-4069, 1993; Huang et al., **Science** 264:961-965, 1994; Macatonia et al., **Journal of Experimental Medicine** 169:1255-1264, 1989; Bhardwaj et al., **Journal of Clinical Investigation** 94:797-807, 1994; and Inaba et al., **Journal of Experimental Medicine** 172:631-640, 1990.

The proteins encoded by the cDNAs may also be evaluated for their influence on the lifetime of lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Darzynkiewicz et al., **Cytometry** 13:795-808, 1992; Gorczyca et al., **Leukemia** 7:659-670, 1993; Gorczyca et al., **Cancer Research** 53:1945-1951, 1993; Itoh et al., **Cell** 66:233-243, 1991; Zacharchuk, **Journal of Immunology** 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., **International Journal of Oncology** 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Those proteins which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis,

myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to regulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models

of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory form of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells in vivo, thereby activating the T cells.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 macroglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class II or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain,can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 34

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Hematopoiesis Regulating Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Johansson et al. **Cellular Biology** 15:141-151, 1995; Keller et al., **Molecular and Cellular Biology** 13:473-486, 1993; McClanahan et al., **Blood** 81:2903-2915, 1993.

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Freshney, M.G. Methylcellulose Colony Forming Assays, in **Culture of Hematopoietic Cells.** R.I. Freshney, et al. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., **Proc. Natl. Acad. Sci. USA** 89:5907-5911, 1992; McNiece, I.K. and Briddell, R.A. Primitive Hematopoietic Colony Forming Cells with High Proliferative Potential, in **Culture of Hematopoietic Cells.** R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., **Experimental Hematology** 22:353-359, 1994; Ploemacher, R.E. Cobblestone Area Forming Cell Assay, In **Culture of Hematopoietic Cells.** R.I. Freshney, et al. Eds. pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Spooncer, E., Dexter, M. and Allen, T. Long Term Bone Marrow Cultures in the Presence of Stromal Cells, in **Culture of Hematopoietic Cells.** R.I. Freshney, et al. Eds.

pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; and Sutherland, H.J. Long Term Culture Initiating Cell Assay, in **Culture of Hematopoietic Cells.** R.I. Freshney, et al. Eds. pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Those proteins which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial. For example, a protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 35

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Tissue Growth

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. WO95/16035, International Patent Publication No. WO95/05846 and International Patent Publication No. WO91/07491.

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Those proteins which are involved in the regulation of tissue growth may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue growth is beneficial. For example, a protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or

nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e., for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as

Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokinc damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 36

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Reproductive Hormones or Cell Movement

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Vale et al., **Endocrinology** 91:562-572, 1972; Ling et al., **Nature** 321:779-782, 1986; Vale et al., **Nature** 321:776-779, 1986; Mason et al., **Nature** 318:659-663, 1985; Forage et al., **Proc. Natl. Acad. Sci. USA** 83:3091-3095, 1986. Chapter 6.12 (Measurement of Alpha and Beta Chemokines) **Current Protocols in Immunology**, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece ; Taub et al. **J. Clin. Invest.** 95:1370-1376, 1995; Lind et al. **APMIS** 103:140-146, 1995; Muller et al. **Eur. J. Immunol.** 25:1744-1748; Gruber et al. **J. of Immunol.** 152:5860-5867, 1994; Johnston et al. **J. of Immunol.** 153:1762-1768, 1994.

Those proteins which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones or cell movement are beneficial. For example, a protein of the present invention may also exhibit activin- or inhibin-related

activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of folic stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 36A

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Chemotactic/Chemokinetic Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for chemotactic/chemokinetic activity. For example, a protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, cosinophils, epithelial and/or endothelial cells. Chemotactic and chmokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods: Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhension of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12,

Measurement of alpha and beta Chemokincs 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Mueller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol, 153:1762-1768, 1994.

EXAMPLE 37

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Blood Clotting

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Linet et al., **J. Clin. Pharmacol.** 26:131-140, 1986; Burdick et al., **Thrombosis Res.** 45:413-419, 1987; Humphrey et al., **Fibrinolysis** 5:71-79 (1991); Schaub, **Prostaglandins** 35:467-474, 1988.

Those proteins which are involved in the regulation of blood clotting may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood clotting is beneficial. For example, a protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as,for example, infarction of cardiac and central nervous system vessels (e.g., stroke). Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 38

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Involvement in Receptor/Ligand Interactions

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 7.28 (Measurement of Cellular Adhesion under Static Conditions 7.28.1-7.28.22) in **Current Protocols in Immunology**, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Takai et al., **Proc. Natl. Acad. Sci. USA** 84:6864-6868, 1987; Bierer et al., **J. Exp. Med.** 168:1145-1156, 1988; Rosenstein et al., **J. Exp. Med.** 169:149-160, 1989; Stoltenborg et al., **J. Immunol. Methods** 175:59-68, 1994; Stitt et al., **Cell** 80:661-670, 1995; Gyuris et al., *Cell* 75:791-803, 1993.

For example, the proteins of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion

molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune respones). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

EXAMPLE 38A

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Anti-Inflammatory Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)),ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

EXAMPLE 38B

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Tumor Inhibition Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, climinating or inhibiting factors, agents or cell types which promote tumor growth.

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or

circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or climination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

EXAMPLE 39

Identification of Proteins which Interact with Polypeptides Encoded by Extended cDNAs

Proteins which interact with the polypeptides encoded by extended cDNAs or portions thereof, such as receptor proteins, may be identified using two hybrid systems such as the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech), the extended cDNAs or portions thereof, are inserted into an expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast transcriptional activator GAL4. cDNAs in a cDNA library which encode proteins which might interact with the polypeptides encoded by the extended cDNAs or portions thereof are inserted into a second expression vector such that they are in frame with DNA encoding the activation domain of GAL4. The two expression plasmids are transformed into yeast and the yeast are plated on selection medium which selects for expression of selectable markers on each of the expression vectors as well as GAL4 dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine are screened for GAL4 dependent lacZ expression. Those cells which are positive in both the histidine selection and the lacZ assay contain plasmids encoding proteins which interact with the polypeptide encoded by the extended cDNAs or portions thereof.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99 (1997) may be used for identifying molecules which interact with the polypeptides encoded by extended cDNAs. In such systems, *in vitro* transcription reactions are performed on a pool of vectors containing extended cDNA inserts cloned downstream of a promoter which drives *in vitro* transcription. The resulting pools of mRNAs are introduced into *Xenopus laevis* oocytes. The oocytes are then assayed for a desired acitivity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro.* The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known polypeptide.

Proteins or other molecules interacting with polypeptides encoded by extended cDNAs can be found by a variety of additional techniques. In one method, affinity columns containing the polypeptide encoded by the extended cDNA or a portion thereof can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein encoded by the extended cDNA or a portion thereof is fused to glutathione S-transferase. A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Proteins interacting with the polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunsen et al. Electrophoresis, 18, 588-598 (1997). Alternatively, the proteins retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

Proteins interacting with polypeptides encoded by extended cDNAs or portions thereof can also be screened by using an Optical Biosensor as described in Edwards & Leatherbarrow, Analytical Biochemistry, 246, 1-6 (1997). The main advantage of the method is that it allows the determination of the association rate between the protein and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymethl dextran matrix) and a sample of test molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extend a few hundred manometers from the sensor surface). In these screening assays, the target molecule can be one of the polypeptides encoded by extended cDNAs or a portion thereof and the test sample can be a collection of proteins extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or chemical libraries,or phage displayed peptides. The tissues or cells from which the test proteins are extracted can originate from any species.

In other methods, a target protein is immobilized and the test population is a collection of unique polypeptides encoded by the extended cDNAs or portions thereof.

To study the interaction of the proteins encoded by the extended cDNAs or portions thereof with drugs, the microdialysis coupled to HPLC method described by Wang et al., Chromatographia, 44, 205-208(1997) or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328 (1997), the disclosures of which are incorporated herein by referenc can be used.

The system described in U.S. Patent No. 5,654,150 may also be used to identify molecules which interact with the polypeptides encoded by the extended cDNAs. In this system, pools of extended cDNAs are transcribed and translated *in vitro* and the reaction products are assayed for interaction with a known polypeptide or antibody.

It will be appreciated by those skilled in the art that the proteins expressed from the extended cDNAs or portions may be assayed for numerous activities in addition to those specifically enumerated above. For example, the expressed proteins may be evaluated for applications involving control and regulation of inflammation, tumor

proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins expressed from the extended cDNAs or portions thereof may be useful as nutritional agents or cosmetic agents.

The proteins expressed from the extended cDNAs or portions thereof may be used to generate antibodies capable of specifically binding to the expressed protein or fragments thereof as described in Example 40 below. The antibodies may capable of binding a full length protein encoded by one of the sequences of SEQ ID NOs. 40-140 and 242-377, a mature protein encoded by one of the sequences of SEQ ID NOs. 40-140 and 242-377, or a signal peptide encoded by one of the sequences of SEQ ID Nos. 40-140 and 242-377. Alternatively, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 10 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 15 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In further embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 40 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513.

EXAMPLE 40

Production of an Antibody to a Human Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells as described in Example 30. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

A. Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., **Nature 256**:495 (1975) or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as Elisa, as originally described by Engvall, E., **Meth. Enzymol. 70**:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. **Basic Methods in Molecular Biology** Elsevier, New York. Section 21-2.

B. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. **J. Clin. Endocrinol. Metab.** 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: **Handbook of Experimental Immunology** D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 μM). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: **Manual of Clinical Immunology**, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

V. Use of Extended cDNAs or Portions Thereof as Reagents

The extended cDNAs of the present invention may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the extended cDNAs (or genomic DNAs obtainable therefrom) may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, sequences from the extended cDNAs (or genomic DNAs obtainable therefrom) may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

EXAMPLE 41

Preparation of PCR Primers and Amplification of DNA

The extended cDNAs (or genomic DNAs obtainable therefrom) may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and forensic techniques. The PCR primers are at least 10 bases, and preferably at least 12, 15, or 17 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C

ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

EXAMPLE 42

Use of Extended cDNAs as Probes

Probes derived from extended cDNAs or portions thereof (or genomic DNAs obtainable therefrom) may be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including in vitro transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or in vitro transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 30 above.

PCR primers made as described in Example 41 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 43-47 below. Such analyses may utilize detectable probes or primers based on the sequences of the extended cDNAs isolated using the 5' ESTs (or genomic DNAs obtainable therefrom).

EXAMPLE 43

Forensic Matching by DNA Sequencing

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the extended cDNAs (or

genomic DNAs obtainable therefrom), is then utilized in accordance with Example 41 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example, with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

EXAMPLE 44

Positive Identification by DNA Sequencing

The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of sequences from Table IV and the appended sequence listing. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 41. Each of these DNA segments is sequenced, using the methods set forth in Example 43. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

EXAMPLE 45

Southern Blot Forensic Identification

The procedure of Example 44 is repeated to obtain a panel of at least 10 amplified sequences from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200 amplified sequences. This PCR-generated DNA is then digested with one or a combination of, preferably, four base specific restriction enzymes. Such enzymes are commercially available and known to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple duplicate wells on an agarose gel and transferred to nitrocellulose using Southern blotting techniques well known to those with skill in the art. For a review of Southern blotting see Davis et al. (**Basic Methods in Molecular Biology**, 1986, Elsevier Press. pp 62-65).

A panel of probes based on the sequences of the extended cDNAs (or genomic DNAs obtainable therefrom), or fragments thereof of at least 10 bases, are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis et al., supra). Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30

nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of extended cDNAs (or genomic DNAs obtainable therefrom) will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of extended cDNA probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

EXAMPLE 46

Dot Blot Identification Procedure

Another technique for identifying individuals using the extended cDNA sequences disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Oligonucleotide probes of approximately 30 bp in length are synthesized that correspond to at least 10, preferably 50 sequences from the extended cDNAs or genomic DNAs obtainable therefrom. The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P^{32} using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and hybridized with labeled probe using techniques known in the art (Davis et al. supra). The ^{32}P labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA. Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., **Proc. Natl. Acad. Sci. USA** 82(6):1585-1588 (1985)). A unique pattern of dots distinguishes one individual from another individual.

Extended cDNAs or oligonucleotides containing at least 10 consecutive bases from these sequences can be used as probes in the following alternative fingerprinting technique. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, a plurality of probes having sequences from different genes are used in the alternative fingerprinting technique. Example 47 below provides a representative alternative fingerprinting procedure in which the probes are derived from extended cDNAs.

EXAMPLE 47

Alternative "Fingerprint" Identification Technique

20-mer oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, of extended cDNA sequences (or genomic DNAs obtainable therefrom) using commercially available oligonucleotide services such as Genset, Paris, France. Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and XbaI. Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with P^{32}. The nitrocellulose is prehybridized with blocking solution and hybridized with the labeled probes. Following hybridization and washing, the nitrocellulose filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

The antibodies generated in Examples 30 and 40 above may be used to identify the tissue type or cell species from which a sample is derived as described above.

EXAMPLE 48

Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of antibody preparations according to Examples 30 and 40 which are conjugated, directly or indirectly to a detectable marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semi-qualitative interpretation.

Antisera for these procedures must have a potency exceeding that of the native preparation, and for that reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ion-exchange chromatography or by ammonium sulfate fractionation. Also, to provide the most specific antisera, unwanted antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous antisera is suitable for either procedure.

A. Immunohistochemical Techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, H., Chap. 26 in: **Basic 503 Clinical Immunology**, 3rd Ed. Lange, Los Altos, California (1980) or Rose, N. et al., Chap. 12 in: **Methods in Immunodiagnosis**, 2d Ed. John Wiley 503 Sons, New York (1980).

A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example ^{125}I, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 μm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

B. Identification of Tissue Specific Soluble Proteins

The visualization of tissue specific proteins and identification of unknown tissues from that procedure is carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however the sample is prepared according to an electrophoretic technique to distribute the proteins extracted from the tissue in an orderly array on the basis of molecular weight for detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice

in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, L. et al., Section 19-2 in: **Basic Methods in Molecular Biology** (P. Leder, ed), Elsevier, New York (1986), using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to55 µl, and containing from about 1 to 100 µg protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., (above) Section 19-3. One set of nitrocellulose blots is stained with Coomassie Blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 30 and 40. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure A or B, a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled; alternatively, the unlabeled complex can be bound by a labeled secondary anti-IgG antibody. In other approaches, either the primary or secondary antibody is conjugated to a biotin molecule, which can, in a subsequent step, bind an avidin conjugated marker. According to yet another strategy, enzyme labeled or radioactive protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, prepared from the gene sequences identified from extended cDNA sequences, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign bodily sites.

In addition to their applications in forensics and identification, extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to their chromosomal locations. Example 49 below describes radiation hybrid (RH) mapping of human chromosomal regions using extended cDNAs. Example 50 below describes a representative procedure for mapping an extended cDNA (or a genomic DNA obtainable therefrom) to its location on a human chromosome. Example 51 below describes mapping of extended cDNAs (or genomic DNAs obtainable therefrom) on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH).

EXAMPLE 49

Radiation hybrid mapping of Extended cDNAs to the human genome

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al. (*Genomics* **4**:509-517, 1989) and Cox et al., (*Science* **250**:245-250, 1990). The random and independent nature of the subclones permits efficient mapping of any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering extended cDNAs (or genomic DNAs obtainable therefrom). In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has been done using conventional ESTs (Schuler et al., *Science* **274**:540-546, 1996).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thymidine kinase (TK) (Foster et al., *Genomics* **33**:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., *Eur. J. Hum. Genet.* **4**:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., *Genomics* **29**:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., *Genomics* **14**:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., *Genomics* **11**:701-708, 1991).

EXAMPLE 50

Mapping of Extended cDNAs to Human Chromosomes using PCR techniques

Extended cDNAs (or genomic DNAs obtainable therefrom) may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from the extended cDNA sequence (or the sequence of a genomic DNA obtainable therefrom) to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich, H.A., PCR Technology; Principles and Applications for DNA Amplification. 1992. W.H. Freeman and Co., New York.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 μCu of a ^{32}P-labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the extended cDNA from which the primers are derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids, BIOS

PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given extended cDNA (or genomic DNA obtainable therefrom). DNA is isolated from the somatic hybrids and used as starting templates for PCR reactions using the primer pairs from the extended cDNAs (or genomic DNAs obtainable therefrom). Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the extended cDNA (or genomic DNA obtainable therefrom) will yield an amplified fragment. The extended cDNAs (or genomic DNAs obtainable therefrom) are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that extended cDNA (or genomic DNA obtainable therefrom). For a review of techniques and analysis of results from somatic cell gene mapping experiments. (See Ledbetter et al., **Genomics** 6:475-481 (1990).)

Alternatively, the extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to individual chromosomes using FISH as described in Example 51 below.

EXAMPLE 51

Mapping of Extended 5' ESTs to Chromosomes Using Fluorescence in situ Hybridization

Fluorescence in situ hybridization allows the extended cDNA (or genomic DNA obtainable therefrom) to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of an extended cDNA (or genomic DNA obtainable therefrom) is obtained by FISH as described by Cherif et al. (*Proc. Natl. Acad. Sci. U.S.A.*, 87:6639-6643, 1990). Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 μM) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BudR, 0.1 mM) for 6 h. Colcemid (1 μg/ml) is added for the last 15 min before harvesting the cells. Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCl (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The extended cDNA (or genomic DNA obtainable therefrom) is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research Laboratories, Bethesda, MD), purified using a Sephadex G-50 column (Pharmacia, Upssala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 X SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100 μg/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at

70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 μg/100 ml in 20 mM Tris-HCl, 2 mM $CaCl_2$) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., *supra.*). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular extended cDNA (or genomic DNA obtainable therefrom) may be localized to a particular cytogenetic R-band on a given chromosome.

Once the extended cDNAs (or genomic DNAs obtainable therefrom) have been assigned to particular chromosomes using the techniques described in Examples 49-51 above, they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a sample.

EXAMPLE 52

Use of Extended cDNAs to Construct or Expand Chromosome Maps

Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the extended cDNAs (or genomic DNAs obtainable therefrom) are obtained. This approach is described in Ramaiah Nagaraja et al. **Genome Research** 7:210-222, March 1997. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the extended cDNA (or genomic DNA obtainable therefrom) whose position is to be determined. Once an insert has been found which includes the extended cDNA (or genomic DNA obtainable therefrom), the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the extended cDNA (or genomic DNA obtainable therefrom) was derived. This process can be repeated for each insert in the YAC library to determine the location of each of the extended cDNAs (or genomic DNAs obtainable therefrom) relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms chromosomes may be obtained.

As described in Example 53 below extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

EXAMPLE 53

Identification of genes associated with hereditary diseases or drug response

This example illustrates an approach useful for the association of extended cDNAs (or genomic DNAs obtainable therefrom) with particular phenotypic characteristics. In this example, a particular extended cDNA (or genomic DNA obtainable therefrom) is used as a test probe to associate that extended cDNA (or genomic DNA obtainable therefrom) with a particular phenotypic characteristic.

Extended cDNAs (or genomic DNAs obtainable therefrom) are mapped to a particular location on a human chromosome using techniques such as those described in Examples 49 and 50 or other techniques known in the art. A search of Mendelian Inheritance in Man (V. McKusick, **Mendelian Inheritance in Man** (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the extended cDNA (or genomic DNA obtainable therefrom) to be a very gene rich region containing several known genes and several diseases or phenotypes for which genes have not been identified. The gene corresponding to this extended cDNA (or genomic DNA obtainable therefrom) thus becomes an immediate candidate for each of these genetic diseases.

Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the extended cDNA (or genomic DNA obtainable therefrom) are used to screen genomic DNA, mRNA or cDNA obtained from the patients. Extended cDNAs (or genomic DNAs obtainable therefrom) that are not amplified in the patients can be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the extended cDNA may be responsible for the genetic disease.

VI. Use of Extended cDNAs (or genomic DNAs obtainable therefrom) to Construct Vectors

The present extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to construct secretion vectors capable of directing the secretion of the proteins encoded by genes inserted in the vectors. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 54 below.

EXAMPLE 54

Construction of Secretion Vectors

The secretion vectors of the present invention include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from an extended cDNA (or genomic DNA obtainable therefrom), such as one of the signal sequences in SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above, is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal peptide encoded by the signal sequence in the

extended cDNA (or genomic DNA obtainable therefrom). Suitable hosts include mammalian cells, tissues or organisms, avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Many nucleic acid backbones suitable for use as secretion vectors are known to those skilled in the art, including retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors, baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and hplc. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

The extended cDNAs or 5' ESTs may also be used to clone sequences located upstream of the extended cDNAs or 5' ESTs which are capable of regulating gene expression, including promoter sequences, enhancer sequences, and other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 55 describes a method for cloning sequences upstream of the extended cDNAs or 5' ESTs.

EXAMPLE 55

Use of Extended cDNAs or 5' ESTs to Clone Upstream Sequences from Genomic DNA

Sequences derived from extended cDNAs or 5' ESTs may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the GenomeWalker™ kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions using an outer adaptor primer provided in the kit and an outer gene specific primer. The gene specific primer should be selected to be specific for the extended cDNA or 5' EST of interest and should have a melting temperature, length, and location in the extended cDNA or ' EST which is consistent with its use in PCR reactions. Each first PCR reaction contains 5ng of genomic DNA, 5 μl of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 μM each of outer adaptor primer and outer gene specific primer, 1.1 mM of $Mg(OAc)_2$, and 1 μl of the Tth polymerase 50X mix in a total volume of 50 μl. The reaction cycle for the first PCR reaction is as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 72°C (7 cycles) / 2 sec @ 94°C, 3 min @ 67°C (32 cycles) / 5 min @ 67°C.

The product of the first PCR reaction is diluted and used as a template for a second PCR reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 μl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 μl volume having a composition identical to that of the first PCR reaction except the nested primers are used. The first nested primer is specific for the adaptor, and is provided with the GenomeWalker™ kit. The second nested primer is specific for the particular extended cDNA or 5' EST for which the promoter is to be cloned and should have a melting temperature, length, and location in the extended cDNA or 5' EST which is consistent with its use in PCR reactions. The reaction parameters of the second PCR reaction are as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 72°C (6 cycles) / 2 sec @ 94°C, 3 min @ 67°C (25 cycles) / 5 min @ 67°C

The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques. Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes. The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 15 nucleotides from the extended cDNA or 5' EST sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing the extended cDNA or EST sequence are isolated as described in Example 29 above. Thereafter, the single stranded DNA containing the extended cDNA or EST sequence is released from the beads and converted into double stranded DNA using a primer specific for the extended cDNA or 5' EST sequence or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. DNAs containing the 5' EST or extended cDNA sequences are identified by colony PCR or colony hybridization.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the extended cDNAs or 5' ESTs with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example 56.

EXAMPLE 56

Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the extended cDNAs or 5' ESTs are cloned into a suitable promoter reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, pβgal-Basic, pβgal-Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline phosphatase, β galactosidase, or green fluorescent protein. The sequences upstream of the extended cDNAs or 5' ESTs are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the inserted upstream sequence.

Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the extended cDNAs and ESTs. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular extended cDNA or 5' EST is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion. The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

EXAMPLE 57

Cloning and Identification of Promoters

Using the method described in Example 55 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA TTG CCT G (SEQ ID NO:29) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ ID NO:30), the promoter having the internal designation P13H2 (SEQ ID NO:31) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:32) and CTG TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:33), the promoter having the internal designation P15B4 (SEQ ID NO:34) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEQ ID NO:35) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:36), the promoter having the internal designation P29B6 (SEQ ID NO:37) was obtained.

Figure 8 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags. The upstream sequences were screened for the presence of motifs resembling transcription factor binding sites or known transcription start sites using the computer program MatInspector release 2.0, August 1996.

Figure 9 describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the MatInspector matrix used. The column labeled position provides the 5' postion of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the MatInspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of the site found.

The promoters and other regulatory sequences located upstream of the extended cDNAs or 5' ESTs may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described in Example 26 above. For example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of an extended cDNA or 5' EST derived from an mRNA which is expressed at a high level in muscle, as determined by the method of Example 26, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences using the procedures of Examples 55-57, proteins which interact with the promoter may be identified as described in Example 58 below.

EXAMPLE 58

Identification of Proteins Which Interact with Promoter Sequences, Upstream Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assessed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art. Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit avalilabe from Clontech (Catalog No. K1603-1). Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem.

A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or in vitro transcription vectors. Binding of the polypeptides encoded by the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

VII. Use of Extended cDNAs (or Genomic DNAs Obtainable Therefrom) in Gene Therapy

The present invention also comprises the use of extended cDNAs (or genomic DNAs obtainable therefrom) in gene therapy strategies, including antisense and triple helix strategies as described in Examples 57 and 58 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes

to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

EXAMPLE 59

Preparation and Use of Antisense Oligonucleotides

The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom). The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an intracellular duplex having sufficient stability to inhibit the expression of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., **Ann. Rev. Biochem.** 55:569-597 (1986) and Izant and Weintraub, **Cell** 36:1007-1015 (1984).

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the opposite strand from that which is normally transcribed in the cell. The antisense molecules may be transcribed using in vitro transcription systems such as those which employ T7 or SP6 polymerase to generate the transcript. Another approach involves transcription of the antisense nucleic acids in vivo by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

Alternatively, oligonucleotides which are complementary to the strand normally transcribed in the cell may be synthesized in vitro. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi et al., **Pharmacol. Ther. 50**(2):245-254, (1991).

Various types of antisense oligonucleotides complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom) may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT WO94/23026 are used. In these moleucles, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523 are used. These double- or single-stranded oligonucleotides comprise one or

more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO 92/18522 may also be used. These molecules are stable to degradation and contain at least one transcription control recognition sequence which binds to control proteins and are effective as decoys therefor. These molecules may contain "hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop" structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2 are used. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732 is also contemplated. Because these molecules have no free ends, they are more resistant to degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using in vitro expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection or transfection using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between $1x10^{-10}$M to $1x10^{-4}$M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use in vivo. For example, an inhibiting concentration in culture of $1x10^{-7}$ translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., *supra*.

In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to antibody-mediated tests such as RIAs and ELISA, functional assays, or radiolabeling.

The extended cDNAs of the present invention (or genomic DNAs obtainable therefrom) may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The extended cDNAs (or genomic DNAs obtainable therefrom) of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, a portion of the extended cDNA (or genomic DNA obtainable therefrom) can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences from the extended cDNA or from the gene corresponding to the extended cDNA are contemplated within the scope of this invention.

EXAMPLE 60

Preparation and use of Triple Helix Probes

The sequences of the extended cDNAs (or genomic DNAs obtainable therefrom) are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches which could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into tissue culture cells which normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target gene in cells which have been treated with the oligonucleotide . The cell functions to be monitored are predicted based upon the homologies of the target gene corresponding to the extended cDNA from which the oligonucleotide was derived with known gene sequences that have been associated with a particular function. The cell functions can also be

predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the extended cDNA is associated with the disease using techniques described in Example 53.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced in vivo using the techniques described above and in Example 59 at a dosage calculated based on the in vitro results, as described in Example 59.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (**Science 245**:967-971 (1989).

EXAMPLE 61

Use of Extended cDNAs to Express an Encoded Protein in a Host Organism

The extended cDNAs of the present invention may also be used to express an encoded protein in a host organism to produce a beneficial effect. In such procedures, the encoded protein may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein may have any of the activities described above. The encoded protein may be a protein which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

A full length extended cDNA encoding the signal peptide and the mature protein, or an extended cDNA encoding only the mature protein is introduced into the host organism. The extended cDNA may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the extended cDNA may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors.

The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells in vitro. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein to produce a beneficial effect.

EXAMPLE 62

Use Of Signal Peptides Encoded By 5' Ests Or Sequences Obtained Therefrom To Import Proteins Into Cells

The short core hydrophobic region (h) of signal peptides encoded by the 5'ESTS or extended cDNAs derived from the 5'ESTs of the present invention may also be used as a carrier to import a peptide or a protein of interest, so-

called cargo, into tissue culture cells (Lin *et al., J. Biol. Chem.,* **270**: 14225-14258 (1995); Du *et al., J. Peptide Res.,* **51**: 235-243 (1998); Rojas *et al., Nature Biotech.,* **16**: 370-375 (1998)).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the h region to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the h region to the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either *in vitro* or *in vivo* after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin *et al., supra*; Lin *et al., J. Biol. Chem.,* **271**: 5305-5308 (1996); Rojas *et al., J. Biol. Chem.,* **271**: 27456-27461 (1996); Liu *et al., Proc. Natl. Acad. Sci. USA*, **93**: 11819-11824 (1996); Rojas *et al., Bioch. Biophys. Res. Commun.,* **234**: 675-680 (1997)).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the host organism.

Alternatively, the h region of signal peptides of the present invention could be used in combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such oligonucleotides may be antisense oligonucleotides or oligonucleotides designed to form triple helixes, as described in examples 59 and 60 respectively, in order to inhibit processing and maturation of a target cellular RNA.

EXAMPLE 63

Reassembling & Resequencing of Clones

Full length cDNA clones obtained by the procedure described in Example 27 were double-sequenced. These sequences were assembled and the resulting consensus sequences were then reanalyzed. Open reading frames were reassigned following essentially the same process as the one described in Example 27.

After this reanalysis process a few abnormalities were revealed. The sequences presented in SEQ ID NOs: 47, 73, 79, 89, 91, 96, 126, 128, 134, and 139 are apparently unlikely to be genuine full length cDNAs. These clones are missing a stop codon and are thus more probably 3' truncated cDNA sequences. Similarly, the sequences presented in SEQ ID NOs: 45, 50, 54, 57, 73, 74, 89, 92, 95, 98, 126, 129, 130, 131 and 139 may also not be genuine full length cDNAs based on homology studies with existing protein sequences. Although both of these sequences encode a potential start methionine each could represent a 5' truncated cDNA.

In addition, SEQ ID NO: 115 was found to be an alternatively spliced transcript and the identities of some of the bases in SEQ ID NO: 131 were corrected.

Finallly, after the reassignment of open reading frames for the clones, new open reading frames were chosen in some instances. For example, in the case of SEQ ID NOs: 41, 47, 50, 52, 54-56, 58, 59, 61, 74, 75, 79, 84, 89, 91, 92, 96, 98, 103, 105, 106, 126, 129, 131, and 133 the new open reading frames were no longer predicted to contain a signal peptide.

As discussed above, Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEQ ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV) the locations in SEQ ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading g PolyA Signal Location in Table IV) and the locations of polyA sites (listed under the heading PolyA Site Location in Table IV).

As discussed above, Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 379-513 in the mature polypeptide created by cleaving the signal peptide from the fall length polypeptide (fourth column). In Table V, and in the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1 and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

EXAMPLE 64

Functional Analysis of Predicted Protein Sequences

Following double-sequencing, new contigs were assembled for each of the extended cDNAs of the present invention and each was compared to known sequences available at the time of filing. These sequences originate from the following databases: Genbank (release 108 and daily releases up to October, 15, 1998), Genseq (release 32) PIR (release 53) and SwissProt (release 35). The predicted proteins of the present invention matching known proteins were further classified into 3 categories depending on the level of homology.

The first category contains proteins of the present invention exhibiting more than 70% identical amino acid residues on the whole length of the matched protein. They are clearly close homologues which most probably have the same function or a very similar function as the matched protein.

The second category contains proteins of the present invention exhibiting more remote homologies (40 to 70% over the whole protein) indicating that the protein of the present inventionmay have functions similar to those of the homologous protein.

The third category contains proteins exhibiting homology (90 to 100%) to a domain of a known protein indicating that the matched protein and the protein of the invention may share similar features.

It should be noted that the numbering of amino acids in the protein sequences discussed in Figures 10 to 15, and Table VIII, the first methionine encountered is designated as amino acid number 1. In the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1, and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

In addition all of the corrected amino acid sequences (SEQ ED NOs: 141-241 and 378-513) were scanned for the presence of known protein signatures and motifs. This search was performed against the Prosite 15.0 database, using the Proscan software from the GCG package. Functional signatures and their locations are indicated in Table VIII.

A) Proteins which are closely related to known proteins

Protein of SEQ ID NO: 217

The protein of SEQ ID NO: 217 encoded by the extended cDNA SEQ ID NO: 116 isolated from lymphocyte shows complete identity to a human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEQ ID NO: 516) as shown by the alignment in figure 10.

Taken together, these data suggest that the protein of SEQ ID NO: 217 may be involved in the control of development and homeostasis. Thus, this protein may be useful in diagnosis and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders, viral infections such as AIDS, neurodegenerative disorders, osteoporosis.

Proteins of SEQ ID NOs: 174, 175 and 232

The proteins of SEQ ID NOs: 174, 175 and 232 encoded by the extended cDNAs SEQ ID NOs:. 73, 74 and 131 respectively and isolated from lymphocytes shows complete extensive homologies to a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517). As shown by the alignments of figure 11, the amino acid residues are identical to those of the 110 amino acid long matched protein except for positions 51 and 108-110 of the matched protein for the protein of SEQ ID NOs: 174, for positions 48, 94 and 108-110 of the matched protein of SEQ ID NOs:175 and for positions 94, and 108-110 of the matched protein for the protein of SEQ ID NOs: 232. Proteins of SEQ ID NOs: 174 and 232 may represent alternative forms issued from alternative use of polyadenylation signals.

Taken together, these data suggest that the proteins of SEQ ID NOs: 174, 175 and 232 may play a role in cell proliferation and/or differentiation, in immune responses and/or in haematopoeisis. Thus, this protein or part therein,

may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection .

Proteins of SEQ ID NO: 231

The protein of SEQ ID NO: 231 encoded by the extended cDNA SEQ ID NO: 130 shows extensive homology with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515). As shown by the alignments in figure 12, the amino acid residues are identical except for position 159 in the 263 amino acid long matched sequence. The matched protein might be involved in the development and differentiation of haematopoietic stem/progenitor cells. In addition, it is the human homologue of a murine protein thought to be involved in chondro-osteogenic differentiation and belonging to a novel multigene family of integral membrane proteins (Deleersnijder *et al, J. Biol. Chem.*, 271 : 19475-19482 (1996)).

The protein of invention contains two short segments from positions 1 to 21 and from 100 to 120 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10 : 685-686 (1994)). The first transmembrane domains matches exactly those predicted for the murine E25 protein.

Taken together, these data suggest that the protein of SEQ ID NO: 231 may be involved in cellular proliferation and differentiation. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and embryogenesis disorders.

Protein of SEQ ID NO: 196

The protein of SEQ ID NO: 196 encoded by the extended cDNA SEQ ID NO: 95 shows extensive homology with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518) and its murine homologue (Genbank accession number Y11550). As shown by the alignments in figure 13, the amino acid residues are identical except for position 174 in the 399 amino acid long human matched sequence. The matched protein potentially associated to stomatin may act as a G-protein coupled receptor and is likely to be important for the signal transduction in neurons and haematopoietic cells (Mayer *et al, Biochem. Biophys. Acta.*, 1395 : 301-308 (1998)).

Taken together, these data suggest that the protein of SEQ ID NOs: 196 may be involved in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases cardiovascular disorders, hypertension, renal injury and repair and septic shock.

Protein of SEQ ID NO: 158

The protein of SEQ ID NOs: 158 encoded by the extended cDNA SEQ ID NO: 57 shows homology with the murine subunit 7a of the COP9 complex (Genbank accession number AF071316, SEQ ID NO: 520). As shown by the

alignments in figure 14, the amino acid residues are identical except for positions 90, 172 and 247 in the 275 amino acid long matched sequence. This complex is highly conserved between mammals and higher plants where it has been shown to act as a repressor of photomorphogenesis All the components of the mammalian COP9 complex contain structural features also present in components of the proteasome regulatory complex and the translation initiation complex eIF3 complex, suggesting that the mammalian COP9 complex is an important cellular regulator modulating multiple signaling pathways (Wei *et al, Curr. Biol.*, **8** : 919-922 (1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 158 may be involved in cellular signaling, probably as a subunit of the human COP9 complex. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

Protein of SEQ ID NO: 226

The protein of SEQ ID NO: 226 encoded by the extended cDNA SEQ ID NO: 125 shows homology with the bovine subunit B14.5B of the NADH-ubiquinone oxidureductase complex (Arizmendi *et al, FEBS Lett.*, **313** : 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514). As shown by the alignments in figure 15, the amino acid residues are identical except for positions 3-4, 6-12, 32-34, 47, 53-55, 67 and 69-74 in the 120 amino acid long matched sequence. This complex is the first of four complexes located in the inner mitochondrial membrane and composing the mitochondrial electron transport chain. Complex I is involved in the dehydrogenation of NADH and the transportation of electrons to coenzyme Q. It is composed of 7 subunits encoded by the mitochondrial genome and 34 subunits encoded by the nuclear genome. It is also thought to play a role in the regulation of apoptosis and necrosis. Mitochondriocytopathies due to complex I deficiency are frequently encountered and affect tissues with a high energy demand such as brain (mental retardation, convulsions, movement disorders), heart (cardiomyopathy, conduction disorders), kidney (Fanconi syndrome), skeletal muscle (exercise intolerance, muscle weakness, hypotonia) and/or eye (opthmaloplegia, ptosis, cataract and retinopathy). For a review on complex I see Smeitink *et al., Hum. Mol. Gent.*, **7** : 1573-1579 (1998).

Taken together, these data suggest that the protein of SEQ ID NO: 226 may be part of the mitochondrial energy-generating system, probably as a subunit of the NADH-ubiquinone oxidoreductase complex. Thus, this protein or part therein, may be useful in diagnosing and/or treating several disorders including, but not limited to, brain disorders (mental retardation, convulsions, movement disorders), 'heart disorders (cardiomyopathy, conduction disorders), kidney disorders (Fanconi syndrome), skeletal muscle disorders (exercise intolerance, muscle weakness, hypotonia) and/or eye disorders opthmalmoplegia, ptosis, cataract and retinopathy).

B) Proteins which are remotely related to proteins with known functions

Proteins of SEQ ID NOs: 149, 150 and 211

The proteins of SEQ ID NOs: 1.49,150 and 211 encoded by the extended cDNAs SEQ ID NOs: 48, 49 and 110 respectively and found in, skeletal muscle shows homologies with T1/ST2 ligand polypeptide of either human (Genbank accession number U41804 and Genseq accession number W09639) or rodent species (Genbank accession number U41805 and Genseq accession number W09640). These polypeptides are thought to be cytokines that bind to the ST2 receptor, a member of the immunoglobulin family homologous to the interleukin-1 receptor and present on some lymphoma cells. They are predicted to be cell-surface proteins containing a short transmembrane domain. (Gayle *et al, J. Biol. Chem.*, 271 : 5784-5789 (1996)). Proteins of SEQ ID NOs: 149, 150 and 211 may represent alternative forms issued from alternative use of polyadenylation signals.

The protein of invention contains two short transmembrane segments from positions 5 to 25 and from 195 to 215 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10 :685-686 (1994)). The second transmembrane domain matches exactly those of the matched cell-surface protein.

Taken together, these data suggest that the protein of SEQ ID NOs: 149, 150 and 211 may act as a cytokine, thus may play a role in the regulation of cell growth and differentiation and/or in the regulation of the immune response. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents such as HIV and/or to suppress graft rejection.

Protein of SEQ ID NO: 177

The protein SEQ ID NO: 177 found in testis encoded by the extended cDNA SEQ ID NO: 76 shows homologies to serine protease inhibitor proteins belonging to the pancreatic trypsin inhibitor family (Kunitz) such as the extracellular proteinase inhibitor named chelonianin (Swissprot accession number P00993). The characteristic PROSITE signature of this family is conserved in the protein of the invention (positions 69 to 87) except for a drastic change of the last cysteine residue into an arginine residue.

Taken together, these data suggest that the protein of SEQ ID NO: 177 may be a protease inhibitor, probably of the Kunitz family. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including but not limited to, cancer and neurodegenerative disorders such as Alzheimer's disease.

Protein of SEQ ID NO: 146

The protein SEQ ID NO: 146 encoded by the extended cDNA SEQ ID NO: 45 shows homology to human apolipoprotein L (Genbank accession number AF019225). The matched protein is a secreted high density lipoprotein associated with apoA-I-containing lipoproteins which play a key role in reverse cholesterol transport.

Taken together, these data suggest that the protein of SEQ ID NO. 146 may play a role in lipid metabolism. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to,

hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as, coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia.

Protein of SEQ ID NO: 163

The protein SEQ ED NO: 163 encoded by the extended cDNA SEQ ID NO: 62 shows homology to the yeast autophagocytosis protein AUT1 (SwissProt accession number P40344). The matched protein is required for starvation-induced non-specific bulk transport of cytoplasmic proteins to the vacuole.

Taken together, these data suggest that the protein of SEQ ID NO: 163 may play a role in protein transport. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

C) Proteins homologous to a domain of a protein with known function

Protein of SEQ ID NO: 214

The protein of SEQ ID NO: 214 encoded by the extended cDNA SEQ ID NO: 113 and expressed in adult brain shows extensive homology to part of the murine SHYC protein (Genbank accession number AF072697) which is expressed in the developing and embryonic nervous system as well as along the olfactory pathway in adult brains (Köster *et al., Neuroscience Letters.*, 252 : 69-71 (1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system development and function. Thus, this protein may be useful in diagnosing and/or treating cancer and/or brain disorders, including neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.

Protein of SEQ ID NO: 225

The protein of SEQ ID NO: 225 encoded by the extended cDNA SEQ ID NO: 124 and expressed in adult prostate belong to the phosphatidylethanolainin-binding protein from which it exhibits the characteristic PROSITE signature from positions 90 to 112 (see table VIII). Proteins from this widespread family, from nematodes to fly, yeast, rodent and primate species, bind hydrophobic ligands such as phospholipids and nucleotides. They are mostly expressed in brain and in testis and are thought to play a role in cell growth and/or maturation, in regulation of the sperm maturation, motility and 'in membrane remodeling. They may act either through signal transduction or through oxidoreduction reactions (for a review see Schoentgen and Jollès, *FEBS Letters*, 369 : 22-26 (1995)).

Taken together, these data suggest that the protein of SEQ ID NO: 225 may play a role in cell. Thus, these growth, maturation and in membrane remodeling and/or may be related to male fertility. Thus, this protein may be useful in diagnosing and/or treating cancer, neurodegenerative diseases, and/of, disorders related to male fertility and sterility.

Protein of SEQ ID NO: 153

The protein of SEQ ID NO: 153 encoded by the extended cDNA SEQ ID NO. 52 and expressed in brain exhibits homology to different integral membrane proteins. These membrane proteins include the nematode protein SRE-2 (Swissprot accession number Q09273) that belongs to the multigene SRE family of *C. elegans* receptor-like proteins and a family of tricarboxylate carriers conserved between flies and mammals. One member of this matched family is the rat tricarboxylate carrier (Genbank accession number S70011), an anion transporter localized in the inner membrane of mitochondria and involved in the biosynthesis of fatty acids and cholesterol. The protein of the invention contains a short transmembrane segments from positions 5 to 25 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10 :685-686 (1994)).

Taken together, these data suggest that the protein of SEQ ID NO: 153 may play a role in signal transduction and/or in molecule transport. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, immune disorders, cardiovascular disorders, hypertension, renal injury and repair and septic shock

Protein of SEQ ID NO: 213

The protein of SEQ ID NO: 213 encoded by the extended cDNA SEQ ID NO: 112 and expressed in brain exhibits homology with part of the tRNA pseudouridine 55 synthase found in *Escherichia Coli* (Swissprot accession number P09171). This bacterial protein belongs to the NAP57/CBF5/TRUB family of nucleolar proteins found in bacteria, yeasts and mammals involved in rRNA or tRNA biosynthesis, ribosomal subunit assembly and/or centromere/mircotubule binding.

Taken together, these data suggest that the protein of SEQ ID NO: 213 may play a role in rRNA or tRNA biogensis and function. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, hearing loss or disorders linked to chromosomal instability such as dyskeratosis.

Protein of SEQ ED NO: 240

The protein of SEQ ID NO: 240 encoded by the extended cDNA SEQ ID NO: 139 and expressed in brain exhibits homology with a family of eukaryotic cell surface antigens containing 4 transmembrane domains. The PROSITE signature for this family is conserved in the protein of the invention except for a substitution of an alanine residue in place of any of the following hydrophic residues : leucine, valine, isoleucine or methionine (positions 21 to 36).

The protein of the invention contains three short transmembrane segments from positions 6 to 26, 32 to 52 and from 56 to 76 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10 : 685-686 (1994)). These transmembrane domains match the last three transmembrane domains of the matched protein family.

Taken together, these data suggest that the protein of SEQ ID NO: 240 may play a role in immunological and/or inflammatory responses, probably as a cell surface antigen. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or

inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection.

Protein of SEQ ID NO: 239

The protein of SEQ ID NO: 239 encoded by the extended cDNA SEQ ID NO: 138 exhibits homology with a conserved region in a family of NA+/H+ exchanger conserved in yeast, nematode and mammals. These cation/proton exchangers are integral membrane proteins with 5 transmembrane segments involved in intracellular pH regulation, maintenance of cell volume, reabsorption of sodium across specialized epithelia, vectorial transport and are also thought to play a role in signal transduction and especially in the induction of cell proliferation and in the induction of apoptosis.

The protein of invention contains four short transmembrane segments from positions 21 to 41, 48 to 68 and from 131 to 151 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, **10** : 685-686 (1994)). The third and fourth transmembrane domains match the fourth and fifth transmembrane segments of the matched family of proteins.

Taken together, these data suggest that the protein of SEQ ID NO: 239 may play a role in membrane permeability and/or in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair, septic shock as well as disorders of membrane permeability such as diarrhea.

Protein of SEQ ID NO: 200

The protein of SEQ ID NO: 200 encoded by the extended cDNA SEQ ED NO: 99 and expressed in brain exhibits extensive homology to the N-terminus of cell division cycle protein 23 (Genbank accession number AF053977) and also to a lesser extent to its homologue in *Saccharomyces cerevisiae*. The matched protein is required for chromosome segregation and is part of the anaphae-promoting complex necessary for cell cycle progression to mitosis.

Taken together, these data suggest that the protein of SEQ ID NO: 200 may play a role in cellular mitosis. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and leukemia.

Protein of SEQ ID NO: 230

The protein of SEQ ID NO: 230 encoded by the extended cDNA SEQ ID NO: 129 exhibits extensive homology to the C-terminus of the eta subunit of T-complex polypeptide 1 conserved from yeasts to mammals, and even complete identity with the last 54 amino acid residues of the human protein (Genbank accession number AF026292). The matched protein is a chaperonin which assists the folding of actins and tubulins in eukaryotic cells upon ATP hydrolysis.

Taken together, these data suggest that the protein of SEQ ID NO: 230 may play a role in the folding, transport, assembly and degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several

types of disorders including, but not limited to, cancer, cardiovascular disorders, immune disorders, neurodegenerative disorders, osteoporosis and arthritis.

Protein of SEQ ED NO: 167

The protein of SEQ ID NO: 167 encoded by the extended cDNA SEQ ID NO: 66 exhibits homology to a monkey pepsinogen A-4 precursor (Swissprot accession number P27678) and to related members of the aspartyl protease family. The matched protein belongs to a family of widely distributed proteolytic enzymes known to exist in vertebrate, fungi, plants, retroviruses and some plant viruses.

Taken together, these data suggest that the protein of SEQ ID NO: 167 may play a role in the degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

Protein of SEQ ID NO: 179

The protein of SEQ ID NO: 179 encoded by the extended cDNA SEQ ID NO: 78 found in testis exhibits homology to part of mammalian colipase precursors. Colipases are secreted cofactors for pancreatic lipases that allow the lipase to anchor at the water-lipid interface. Colipase plays a crucial role in the intestinal digestion and absorption of dietary fats. The 5 cysteines characteristic for this protein family are conserved in the protein of the invention although the colipase PROSITE signature is not.

Taken together, these data suggest that the protein of SEQ ED NO: 179 may play a role in the lipid metabolism and/or in male fertility. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia, and disorders linked to male fertility.

Protein of SEQ ID NO: 227

The protein of SEQ ID NO: 227 encoded by the extended cDNA SEQ ID NO: 126 exhibits extensive homology to the ATP binding region of a whole family of serine/threonine protein kinases belonging to the CDC2/CDC28 subfamily. The PROSITE signature characteristic for this domain is present in the protein of the invention from positions 10 to 34.

Taken together, these data suggest that the protein of SEQ ED NO: 158 may bind ATP, and even be a protein kinase. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims.

As discussed above, the extended cDNAs of the present invention or portions thereof can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning; A Laboratory Manual", 2d ed., Cole Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology; Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a

nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

SEQUENCE LISTING FREE TEXT

The following free text appears in the accompanying Sequence Listing:

In vitro transcription product

oligonucleotide

promoter

transcription start site

Von Heijne matrix

Score

matinspector prediction

name

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TABLE II : Parameters used for each step of EST analysis

	Search Characteristics			Selection Characteristics	
Step	Program	Strand	Parameters	Identity (%))	Length (bp)
Miscellaneous	Blastn	both	S=61 X=16	90	17
tRNA	Fasta	both	-	80	60
rRNA	Blastn	both	S=108	80	40
mtRNA	Blastn	both	S=108	80	40
Procaryotic	Blastn	both	S=144	90	40
Fungal	Blastn	both	S=144	90	40
Alu	fasta*	both	-	70	40
L1	Blastn	both	S=72	70	40
Repeats	Blastn	both	S=72	70	40
Promoters	Blastn	top	S=54 X=16	90	15$\perp$
Vertebrate	fasta*	both	S=108	90	30
ESTs	Blatsn	both	S=108 X=16	90	30
Proteins	blastxη	top	E=0.001	-	-

* use "Quick Fast" Database Scanner

$\perp$ alignment further constrained to begin closer than 10bp to EST\5' end

η using BLOSUM62 substitution matrix

TABLE III: Parameters used for each step of extended cDNA analysis

	Search characteristics		Selection characteristics			
Step	Program	Strand	Parameters	Identity (%)	Length (bp)	Comments
miscellaneous*	FASTA	both	-	90	15	
tRNA†	FASTA	both	-	80	90	
rRNA†	BLASTN	both	S=108	80	40	
mtRNA†	BLASTN	both	S=108	80	40	
Procaryotic†	BLASTN	both	S=144	90	40	
Fungal*	BLASTN	both	S=144	90	40	
Alu*	BLASTN	both	S=72	70	40	max 5 matches, masking
L1†	BLASTN	both	S=72	70	40	max 5 matches, masking
Repeats†	BLASTN	both	S=72	70	40	masking
PolyA	BLAST2N	top	W=6,S=10,E=1000	90	8	in the last 20 nucleotides
Polyadenylation signal	-	top	AATAAA allowing 1 mismatch			in the 50 nucleotides preceding the 5' end of the polA
Vertebrate*	BLASTN then FASTA	both	-	90 then 70	30	first BLASTN and then FASTA on matching sequences
ESTs*	BLAST2N	both	-	90	30	
Geneseq	BLASTN	both	W=8, B=10	90	30	
ORF	BLASTP	top	W=8, B=10	-	-	on ORF proteins, max 10 matches
Proteins*	BLASTX	top	E=0.001	70	30	

† steps common to EST analysis and using the same algorithms and parameters

* steps also used in EST analysis but with different algorithms and/or parameters

TABLE IV

Id	FCS Location	SigPep Location	Mature Polypeptide Location	Stop Codon Location	PolyA Signal Location	PolyA Site Location
40	7 through 471	7 through 99	100 through 471	472	537 through 542	554 through 568
41	168 through 332	-	168 through 332	333	557 through 562	-
42	51 through 251	51 through 110	111 through 251	252	849 through 854	882 through 895
43	20 through 613	20 through 82	83 through 613	614	-	-
44	12 through 416	12 through 86	87 through 416	417	425 through 430	445 through 458
45	276 through 1040	276 through 485	486 through 1040	1041	-	2024 through 2036
46	443 through 619	443 through 589	590 through 619	620	-	1267 through 1276
47	206 through 747	-	206 through 747	-	-	-
48	36 through 521	36 through 104	105 through 521	522	528 through 533	548 through 561
49	36 through 395	36 through 104	105 through 395	396	599 through 604	619 through 632
50	21 through 41	-	21 through 41	42	328 through 333	357 through 370
51	35 through 631	35 through 160	161 through 631	632	901 through 906	979 through 994
52	271 through 399	-	271 through 399	400	-	-
53	103 through 252	103 through 213	214 through 252	253	-	588 through 597
54	2 through 460	-	2 through 460	461	713 through 718	735 through 748
55	31 through 231	-	31 through 231	232	769 through 774	690 through 703
56	305 through 565	-	305 through 565	566	694 through 699	713 through 725
57	124 through 873	124 through 378	379 through 873	874	1673 through 1678	1694 through 1705
58	135 through 206	-	135 through 206	207	850 through 855	1056 through 1069
59	135 through 818	-	135 through 818	819	909 through 914	1071 through 1084
60	33 through 290	33 through 92	93 through 290	291	-	-
61	485 through 616	-	485 through 616	617	-	669 through 682
62	54 through 995	54 through 227	228 through 995	996	1130 through 1135	1181 through 1191
63	657 through 923	657 through 896	897 through 923	924	957 through 962	974 through 1008
64	18 through 311	18 through 62	63 through 311	312	-	-
65	151 through 426	151 through 258	259 through 426	427	505 through 510	527 through 538
66	10 through 1062	10 through 57	58 through 1062	1063	1710 through 1715	1735 through 1747
67	78 through 491	78 through 218	219 through 491	492	1652 through 1657	1673 through 1686
68	69 through 371	69 through 287	288 through 371	372	510 through 515	530 through 542
69	2 through 757	2 through 205	206 through 757	758	-	1160 through 1174
70	2 through 1051	2 through 205	206 through 1051	1052	1248 through 1253	1272 through 1285
71	2 through 1171	2 through 205	206 through 1171	1172	1368 through 1373	1386 through 1398
72	42 through 611	42 through 287	288 through 611	612	787 through 792	808 through 821
73	62 through 916	62 through 757	758 through 916	-	-	904 through 916
74	62 through 520	-	62 through 520	521	1124 through 1129	1141 through 1153
75	21 through 167	-	21 through 167	168	-	-
76	22 through 318	22 through 93	94 through 318	319	497 through 502	516 through 526
77	8 through 292	8 through 118	119 through 292	293	317 through 322	339 through 352
78	16 through 378	16 through 84	85 through 378	379	502 through 507	522 through 542

CONT. TABLE IV

79	57 through 233	-	57 through 233	-	-	-
80	83 through 340	83 through 124	125 through 340	341	573 through 578	607 through 660
81	47 through 541	47 through 220	221 through 541	542	-	597 through 605
82	46 through 285	46 through 150	151 through 285	286	364 through 369	385 through 396
83	22 through 240	22 through 84	85 through 240	241	397 through 402	421 through 432
84	89 through 382	-	89 through 382	383	-	408 through 420
85	80 through 415	80 through 142	143 through 415	416	471 through 476	488 through 501
86	152 through 361	152 through 283	284 through 361	362	-	-
87	32 through 307	32 through 70	71 through 307	308	1240 through 1245	1261 through 1272
88	114 through 734	114 through 239	240 through 734	735	768 through 773	793 through 804
89	199 through 802	-	199 through 802	-	780 through 785	791 through 802
90	38 through 1174	38 through 148	149 through 1174	1175	1452 through 1457	1478 through 1490
91	26 through 361	-	26 through 361	-	-	350 through 361
92	3 through 131	-	3 through 131	132	-	591 through 605
93	33 through 185	33 through 80	81 through 185	186	570 through 575	586 through 591
94	184 through 915	184 through 237	238 through 915	916	1119 through 1124	1139 through 1150
95	58 through 1116	58 through 159	160 through 1116	1117	1486 through 1491	1504 through 1513
96	327 through 417	-	327 through 417	-	-	404 through 417
97	63 through 398	63 through 206	207 through 398	399	-	-
98	2 through 163	-	2 through 163	164	488 through 493	511 through 522
99	13 through 465	13 through 75	76 through 465	466	-	-
100	20 through 703	20 through 94	95 through 703	704	1000 through 1005	1023 through 1041
101	103 through 294	103 through 243	244 through 294	295	-	-
102	81 through 518	81 through 173	174 through 518	519	-	-
103	66 through 326	-	66 through 326	327	1066 through 1071	1087 through 1098
104	170 through 289	170 through 250	251 through 289	290	-	-
105	36 through 497	-	36 through 497	498	650 through 655	663 through 685
106	18 through 320	-	18 through 320	321	539 through 544	542 through 554
107	71 through 1438	71 through 136	137 through 1438	1439	1644 through 1649	1665 through 1678
108	25 through 318	25 through 75	76 through 318	319	452 through 457	482 through 494
109	84 through 332	84 through 170	171 through 332	333	-	702 through 714
110	32 through 718	32 through 100	101 through 718	719	770 through 775	793 through 805
111	26 through 481	26 through 88	89 through 481	482	755 through 760	775 through 787
112	26 through 562	26 through 187	188 through 562	563	-	-
113	4 through 810	4 through 279	280 through 810	811	858 through 863	881 through 893
114	55 through 459	55 through 120	121 through 459	460	1444 through 1449	1462 through 1475
115	48 through 248	48 through 161	162 through 248	249	283 through 288	308 through 321
116	25 through 399	25 through 186	187 through 399	400	-	-
117	10 through 1137	10 through 72	73 through 1137	1138	1144 through 1149	1162 through 1173
118	72 through 704	72 through 161	162 through 704	705	772 through 777	-
119	44 through 505	44 through 223	224 through 505	506	-	-
120	25 through 393	25 through 150	151 through 393	394	734 through 739	757 through 770

CONT. TABLE IV

121	58 through 1095	58 through 114	115 through 1095	1096	-	1202 through 1213
122	31 through 660	31 through 90	91 through 660	661	1288 through 1293	1307 through 1318
123	31 through 582	31 through 90	91 through 582	583	816 through 821	840 through 853
124	15 through 695	15 through 80	81 through 695	696	795 through 800	814 through 826
125	74 through 295	74 through 196	197 through 295	296	545 through 550	561 through 571
126	440 through 659	-	440 through 659	-	601 through 606	-
127	38 through 283	38 through 85	86 through 283	284	257 through 262	-
128	121 through 477	121 through 288	289 through 477	-	-	-
129	2 through 163	-	2 through 163	164	292 through 297	310 through 323
130	46 through 675	46 through 87	88 through 675	676	1364 through 1369	1383 through 1392
131	62 through 385	-	62 through 385	386	974 through 979	987 through 999
132	422 through 550	422 through 475	476 through 550	551	-	714 through 725
133	124 through 231	-	124 through 231	232	-	387 through 400
134	131 through 1053	131 through 169	170 through 1053	-	1019 through 1024	-
135	86 through 403	86 through 181	182 through 403	404	1097 through 1102	1117 through 1128
136	37 through 162	37 through 93	94 through 162	163	224 through 229	243 through 254
137	31 through 381	31 through 90	91 through 381	382	-	875 through 886
138	46 through 579	46 through 156	157 through 579	580	-	-
139	92 through 471	92 through 172	173 through 471	-	454 through 459	458 through 471
140	154 through 675	154 through 498	499 through 675	676	819 through 824	838 through 849
242	18 through 173	18 through 77	78 through 173	174	864 through 869	882 through 893
243	17 through 595	17 through 85	86 through 595	596	820 through 825	840 through 851
244	89 through 334	89 through 130	131 through 334	335	462 through 467	484 through 495
245	21 through 614	21 through 83	84 through 614	615	849 through 854	873 through 884
246	94 through 573	94 through 258	259 through 573	574	862 through 867	886 through 897
247	74 through 397	74 through 127	128 through 397	398	472 through 477	507 through 518
248	51 through 242	51 through 116	117 through 242	243	319 through 324	339 through 350
249	111 through 191	111 through 155	156 through 191	192	965 through 970	986 through 996
250	45 through 602	45 through 107	108 through 602	603	828 through 833	850 through 860
251	24 through 560	24 through 101	102 through 560	561	563 through 568	583 through 593
252	109 through 558	109 through 273	274 through 558	559	-	1104 through 1114
253	128 through 835	128 through 220	221 through 835	836	1145 through 1150	1170 through 1181
254	59 through 505	59 through 358	359 through 505	506	1042 through 1047	1062 through 1073
255	1 through 207	1 through 147	148 through 207	208	784 through 789	807 through 818
256	12 through 734	12 through 101	102 through 734	735	914 through 919	961 through 971
257	378 through 518	378 through 467	468 through 518	519	607 through 612	628 through 640
258	110 through 304	110 through 193	194 through 304	305	708 through 713	732 through 743
259	201 through 419	201 through 272	273 through 419	420	601 through 606	627 through 637
260	123 through 302	123 through 176	177 through 302	303	1279 through 1284	1301 through 1312
261	98 through 673	98 through 376	377 through 673	674	-	1025 through 1035
262	17 through 463	17 through 232	233 through 463	464	657 through 662	684 through 696
263	263 through 481	263 through 322	323 through 481	482	-	858 through 868

CONT. TABLE IV

264	42 through 299	42 through 101	102 through 299	300	-	762 through 775
265	198 through 431	198 through 260	261 through 431	432	-	1064 through 1074
266	279 through 473	279 through 362	363 through 473	474	944 through 949	970 through 981
267	12 through 644	12 through 92	93 through 644	645	1002 through 1007	1020 through 1031
268	91 through 459	91 through 330	331 through 459	460	-	1271 through 1281
269	70 through 327	70 through 147	148 through 327	328	1741 through 1746	1763 through 1774
270	12 through 497	12 through 104	105 through 497	498	935 through 940	955 through 967
271	90 through 383	90 through 200	201 through 383	384	609 through 614	632 through 643
272	332 through 541	332 through 376	377 through 541	542	739 through 744	761 through 773
273	43 through 222	43 through 177	178 through 222	223	530 through 535	555 through 566
274	115 through 231	115 through 180	181 through 231	232	419 through 424	445 through 455
275	232 through 384	232 through 300	301 through 384	385	650 through 655	662 through 673
276	143 through 427	143 through 286	287 through 427	428	606 through 611	628 through 639
277	284 through 463	284 through 379	380 through 463	464	-	762 through 772
278	162 through 671	162 through 398	399 through 671	672	805 through 810	830 through 840
279	63 through 632	63 through 308	309 through 632	633	808 through 813	829 through 840
280	21 through 362	21 through 200	201 through 362	363	821 through 826	838 through 849
281	21 through 503	21 through 344	345 through 503	504	1305 through 1310	1330 through 1341
282	1 through 201	1 through 63	64 through 201	202	637 through 642	660 through 671
283	39 through 1034	39 through 134	135 through 1034	1035	1566 through 1571	1587 through 1597
284	69 through 263	69 through 125	126 through 263	264	1173 through 1178	1196 through 1205
285	115 through 285	115 through 204	205 through 285	286	505 through 510	525 through 536
286	90 through 344	90 through 140	141 through 344	345	500 through 505	515 through 527
287	57 through 311	57 through 107	108 through 311	312	467 through 472	482 through 493
288	96 through 302	96 through 182	183 through 302	303	-	501 through 514
289	161 through 526	161 through 328	329 through 526	527	-	799 through 811
290	210 through 332	210 through 299	300 through 332	333	594 through 599	613 through 625
291	212 through 361	212 through 319	320 through 361	362	650 through 655	673 through 684
292	75 through 482	75 through 128	129 through 482	483	595 through 600	618 through 627
293	50 through 631	50 through 244	245 through 631	632	777 through 782	801 through 812
294	154 through 576	154 through 360	361 through 576	577	737 through 742	763 through 775
295	154 through 897	154 through 360	361 through 897	898	1017 through 1022	1044 through 1054
296	146 through 292	146 through 253	254 through 292	293	395 through 400	433 through 444
297	126 through 383	126 through 167	168 through 383	384	726 through 731	743 through 754
298	66 through 497	66 through 239	240 through 497	498	594 through 599	618 through 629
299	49 through 411	49 through 96	97 through 411	412	732 through 737	750 through 763
300	49 through 534	49 through 96	97 through 534	535	593 through 598	612 through 623
301	86 through 415	86 through 145	146 through 415	416	540 through 545	560 through 571
302	56 through 268	56 through 100	101 through 268	269	584 through 589	601 through 612
303	32 through 328	32 through 103	104 through 328	329	508 through 513	528 through 539
304	21 through 527	21 through 95	96 through 527	528	921 through 926	953 through 963
305	147 through 647	147 through 374	375 through 647	648	-	668 through 681

CONT. TABLE IV

306	262 through 471	262 through 306	307 through 471	472	663 through 668	682 through 693
307	74 through 1216	74 through 172	173 through 1216	1217	1627 through 1632	1640 through 1652
308	48 through 164	48 through 89	90 through 164	165	482 through 487	505 through 517
309	185 through 334	185 through 295	296 through 334	335	355 through 360	392 through 405
310	195 through 347	195 through 272	273 through 347	348	1037 through 1042	1071 through 1082
311	90 through 815	90 through 179	180 through 815	816	883 through 888	905 through 916
312	52 through 513	52 through 231	232 through 513	514	553 through 558	572 through 583
313	172 through 438	172 through 354	355 through 438	439	682 through 687	685 through 697
314	148 through 366	148 through 225	226 through 366	367	770 through 775	792 through 803
315	175 through 336	175 through 276	277 through 336	337	-	812 through 823
316	191 through 553	191 through 304	305 through 553	554	766 through 771	804 through 817
317	106 through 603	106 through 216	217 through 603	604	-	1102 through 1112
318	47 through 586	47 through 124	125 through 586	587	1583 through 1588	1614 through 1623
319	99 through 371	99 through 290	291 through 371	372	491 through 496	513 through 524
320	44 through 814	44 through 112	113 through 814	815	-	978 through 989
321	3 through 581	3 through 182	183 through 581	582	-	1006 through 1016
322	107 through 427	107 through 190	191 through 427	428	499 through 504	516 through 529
323	45 through 407	45 through 83	84 through 407	408	1008 through 1013	1032 through 1042
324	201 through 332	201 through 251	252 through 332	333	-	869 through 880
325	217 through 543	217 through 255	256 through 543	544	-	1206 through 1217
326	18 through 446	18 through 140	141 through 446	447	930 through 935	948 through 959
327	29 through 724	29 through 118	119 through 724	725	886 through 891	910 through 920
328	404 through 586	404 through 466	467 through 586	587	1304 through 1309	1334 through 1344
329	331 through 432	331 through 387	388 through 432	433	548 through 553	573 through 585
330	59 through 703	59 through 220	221 through 703	704	886 through 891	903 through 914
331	672 through 752	672 through 722	723 through 752	753	-	1150 through 1161
332	57 through 311	57 through 128	129 through 311	312	332 through 337	351 through 363
333	80 through 232	80 through 127	128 through 232	233	617 through 622	634 through 645
334	91 through 291	91 through 219	220 through 291	292	367 through 372	389 through 400
335	196 through 384	196 through 240	241 through 384	385	461 through 466	485 through 496
336	54 through 590	54 through 227	228 through 590	591	-	955 through 965
337	133 through 846	133 through 345	346 through 846	847	-	890 through 901
338	138 through 671	138 through 248	249 through 671	672	1319 through 1324	1338 through 1347
339	124 through 411	124 through 186	187 through 411	412	948 through 953	971 through 983
340	372 through 494	372 through 443	444 through 494	495	708 through 713	732 through 745
341	112 through 450	112 through 192	193 through 450	451	1053 through 1058	1095 through 1106
342	117 through 866	117 through 170	171 through 866	867	1159 through 1164	1178 through 1190
343	13 through 465	13 through 75	76 through 465	466	1035 through 1040	1060 through 1070
344	2 through 718	2 through 76	77 through 718	719	1170 through 1175	1203 through 1213
345	86 through 709	86 through 361	362 through 709	710	943 through 948	963 through 973
346	63 through 320	63 through 179	180 through 320	321	771 through 776	799 through 810
347	299 through 418	299 through 379	380 through 418	419	739 through 744	762 through 771

CONT. TABLE IV

348	186 through 380	186 through 233	234 through 380	381	383 through 388	396 through 409
349	69 through 458	69 through 233	234 through 458	459	564 through 569	602 through 613
350	12 through 638	12 through 263	264 through 638	639	951 through 956	975 through 985
351	282 through 389	282 through 332	333 through 389	390	1413 through 1418	1437 through 1447
352	208 through 339	208 through 294	295 through 339	340	-	1631 through 1641
353	69 through 557	69 through 224	225 through 557	558	849 through 854	870 through 883
354	134 through 325	134 through 274	275 through 325	326	-	718 through 729
355	78 through 731	78 through 227	228 through 731	732	-	1002 through 1013
356	46 through 693	46 through 90	91 through 693	694	937 through 942	962 through 973
357	126 through 527	126 through 182	183 through 527	528	834 through 839	856 through 867
358	66 through 320	66 through 113	114 through 320	321	490 through 495	508 through 519
359	73 through 948	73 through 159	160 through 948	949	-	1016 through 1028
360	69 through 434	69 through 236	237 through 434	435	419 through 424	441 through 452
361	628 through 804	628 through 711	712 through 804	805	-	864 through 875
362	70 through 366	70 through 108	109 through 366	367	496 through 501	521 through 531
363	70 through 366	70 through 108	109 through 366	367	-	1233 through 1244
364	111 through 434	111 through 185	186 through 434	435	-	618 through 631
365	19 through 567	19 through 63	64 through 567	568	749 through 754	771 through 781
366	19 through 312	19 through 63	64 through 312	313	896 through 901	921 through 931
367	64 through 612	64 through 234	235 through 612	613	-	839 through 849
368	39 through 458	39 through 80	81 through 458	459	613 through 618	633 through 644
369	9 through 185	9 through 50	51 through 185	186	-	906 through 918
370	14 through 316	14 through 121	122 through 316	317	442 through 447	458 through 471
371	70 through 1092	70 through 234	235 through 1092	1093	1475 through 1480	1493 through 1504
372	274 through 597	274 through 399	400 through 597	598	731 through 736	754 through 765
373	230 through 469	230 through 307	308 through 469	470	1004 through 1009	1027 through 1040
374	72 through 545	72 through 203	204 through 545	546	-	1151 through 1162
375	36 through 425	36 through 119	120 through 425	426	1215 through 1220	1240 through 1250
376	155 through 751	155 through 340	341 through 751	752	912 through 917	937 through 947
377	46 through 585	46 through 120	121 through 585	586	584 through 589	606 through 619

TABLE V

Id	Full Length Polypeptide Location	Signal Peptide Location	Mature Polypeptide Location
141	-31 through 124	-31 through -1	1 through 124
142	1 through 55	-	1 through 55
143	-20 through 47	-20 through -1	1 through 47
144	-21 through 177	-21 through -1	1 through 177
145	-25 through 110	-25 through -1	1 through 110
146	-70 through 185	-70 through -1	1 through 185
147	-49 through 10	-49 through -1	1 through 10
148	1 through 180	-	1 through 180
149	-23 through 139	-23 through -1	1 through 139
150	-23 through 97	-23 through -1	1 through 97
151	1 through 7	-	1 through 7
152	-42 through 157	-42 through -1	1 through 157
153	1 through 43	-	1 through 43
154	-37 through 13	-37 through -1	1 through 13
155	1 through 153	-	1 through 153
156	1 through 67	-	1 through 67
157	1 through 87	-	1 through 87
158	-85 through 165	-85 through -1	1 through 165
159	1 through 24	-	1 through 24
160	1 through 228	-	1 through 228
161	-20 through 66	-20 through -1	1 through 66
162	1 through 44	-	1 through 44
163	-58 through 256	-58 through -1	1 through 256
164	-80 through 9	-80 through -1	1 through 9
165	-15 through 83	-15 through -1	1 through 83
166	-36 through 56	-36 through -1	1 through 56
167	-16 through 335	-16 through -1	1 through 335
168	-47 through 91	-47 through -1	1 through 91
169	-73 through 28	-73 through -1	1 through 28
170	-68 through 184	-68 through -1	1 through 184
171	-68 through 282	-68 through -1	1 through 282
172	-68 through 322	-68 through -1	1 through 322
173	-82 through 108	-82 through -1	1 through 108
174	-232 through 53	-232 through -1	1 through 53
175	1 through 153	-	1 through 153
176	1 through 49	-	1 through 49
177	-24 through 75	-24 through -1	1 through 75
178	-37 through 58	-37 through -1	1 through 58
179	-23 through 98	-23 through -1	1 through 98
180	1 through 59	-	1 through 59
181	-14 through 72	-14 through -1	1 through 72
182	-58 through 107	-58 through -1	1 through 107
183	-35 through 45	-35 through -1	1 through 45
184	-21 through 52	-21 through -1	1 through 52
185	1 through 98	-	1 through 98
186	-21 through 91	-21 through -1	1 through 91
187	-44 through 26	-44 through -1	1 through 26
188	-13 through 79	-13 through -1	1 through 79
189	-42 through 165	-42 through -1	1 through 165
190	1 through 201	-	1 through 201

CONT. TABLE V

191	-37 through 342	-37 through -1	1 through 342
192	1 through 112	-	1 through 112
193	1 through 43	-	1 through 43
194	-16 through 35	-16 through -1	1 through 35
195	-18 through 226	-18 through -1	1 through 226
196	-34 through 319	-34 through -1	1 through 319
197	1 through 30	-	1 through 30
198	-48 through 64	-48 through -1	1 through 64
199	1 through 54	-	1 through 54
200	-21 through 130	-21 through -1	1 through 130
201	-25 through 203	-25 through -1	1 through 203
202	-47 through 17	-47 through -1	1 through 17
203	-31 through 115	-31 through -1	1 through 115
204	1 through 87	-	1 through 87
205	-27 through 13	-27 through -1	1 through 13
206	1 through 154	-	1 through 154
207	1 through 101	-	1 through 101
208	-22 through 434	-22 through -1	1 through 434
209	-17 through 81	-17 through -1	1 through 81
210	-29 through 54	-29 through -1	1 through 54
211	-23 through 206	-23 through -1	1 through 206
212	-21 through 131	-21 through -1	1 through 131
213	-54 through 125	-54 through -1	1 through 125
214	-92 through 177	-92 through -1	1 through 177
215	-22 through 113	-22 through -1	1 through 113
216	-38 through 29	-38 through -1	1 through 29
217	-54 through 71	-54 through -1	1 through 71
218	-21 through 355	-21 through -1	1 through 355
219	-30 through 181	-30 through -1	1 through 181
220	-60 through 94	-60 through -1	1 through 94
221	-42 through 81	-42 through -1	1 through 81
222	-19 through 327	-19 through -1	1 through 327
223	-20 through 190	-20 through -1	1 through 190
224	-20 through 164	-20 through -1	1 through 164
225	-22 through 205	-22 through -1	1 through 205
226	-41 through 33	-41 through -1	1 through 33
227	1 through 73	-	1 through 73
228	-16 through 66	-16 through -1	1 through 66
229	-56 through 63	-56 through -1	1 through 63
230	1 through 54	-	1 through 54
231	-14 through 196	-14 through -1	1 through 196
232	1 through 108	-	1 through 108
233	-18 through 25	-18 through -1	1 through 25
234	1 through 36	-	1 through 36
235	-13 through 294	-13 through -1	1 through 294
236	-32 through 74	-32 through -1	1 through 74
237	-19 through 23	-19 through -1	1 through 23
238	-20 through 97	-20 through -1	1 through 97
239	-37 through 141	-37 through -1	1 through 141
240	-27 through 99	-27 through -1	1 through 99
241	-115 through 59	-115 through -1	1 through 59
378	-20 through 32	-20 through -1	1 through 32
379	-23 through 170	-23 through -1	1 through 170
380	-14 through 68	-14 through -1	1 through 68

CONT. TABLE V

381	-21 through 177	-21 through -1	1 through 177
382	-55 through 105	-55 through -1	1 through 105
383	-18 through 90	-18 through -1	1 through 90
384	-22 through 42	-22 through -1	1 through 42
385	-15 through 12	-15 through -1	1 through 12
386	-21 through 165	-21 through -1	1 through 165
387	-26 through 153	-26 through -1	1 through 153
388	-55 through 95	-55 through -1	1 through 95
389	-31 through 205	-31 through -1	1 through 205
390	-100 through 49	-100 through -1	1 through 49
391	-49 through 20	-49 through -1	1 through 20
392	-30 through 211	-30 through -1	1 through 211
393	-30 through 17	-30 through -1	1 through 17
394	-28 through 37	-28 through -1	1 through 37
395	-24 through 49	-24 through -1	1 through 49
396	-18 through 42	-18 through -1	1 through 42
397	-93 through 99	-93 through -1	1 through 99
398	-72 through 77	-72 through -1	1 through 77
399	-20 through 53	-20 through -1	1 through 53
400	-20 through 66	-20 through -1	1 through 66
401	-21 through 57	-21 through -1	1 through 57
402	-28 through 37	-28 through -1	1 through 37
403	-27 through 184	-27 through -1	1 through 184
404	-80 through 43	-80 through -1	1 through 43
405	-26 through 60	-26 through -1	1 through 60
406	-31 through 131	-31 through -1	1 through 131
407	-37 through 61	-37 through -1	1 through 61
408	-15 through 55	-15 through -1	1 through 55
409	-45 through 15	-45 through -1	1 through 15
410	-22 through 17	-22 through -1	1 through 17
411	-23 through 28	-23 through -1	1 through 28
412	-48 through 47	-48 through -1	1 through 47
413	-32 through 28	-32 through -1	1 through 28
414	-79 through 91	-79 through -1	1 through 91
415	-82 through 108	-82 through -1	1 through 108
416	-60 through 54	-60 through -1	1 through 54
417	-108 through 53	-108 through -1	1 through 53
418	-21 through 46	-21 through -1	1 through 46
419	-32 through 300	-32 through -1	1 through 300
420	-19 through 46	-19 through -1	1 through 46
422	-30 through 27	-30 through -1	1 through 27
423	-17 through 68	-17 through -1	1 through 68
424	-17 through 68	-17 through -1	1 through 68
425	-29 through 40	-29 through -1	1 through 40
426	-56 through 66	-56 through -1	1 through 66
427	-30 through 11	-30 through -1	1 through 11
428	-36 through 14	-36 through -1	1 through 14
429	-18 through 118	-18 through -1	1 through 118
430	-65 through 129	-65 through -1	1 through 129
431	-69 through 72	-69 through -1	1 through 72
432	-69 through 179	-69 through -1	1 through 179
433	-36 through 13	-36 through -1	1 through 13
434	-14 through 72	-14 through -1	1 through 72
435	-58 through 86	-58 through -1	1 through 86

CONT. TABLE V

436	-16 through 105	-16 through -1	1 through 105
437	-16 through 146	-16 through -1	1 through 146
438	-20 through 90	-20 through -1	1 through 90
439	-15 through 56	-15 through -1	1 through 56
440	-24 through 75	-24 through -1	1 through 75
441	-25 through 144	-25 through -1	1 through 144
442	-76 through 91	-76 through -1	1 through 91
443	-15 through 55	-15 through -1	1 through 55
444	-33 through 348	-33 through -1	1 through 348
445	-14 through 25	-14 through -1	1 through 25
446	-37 through 13	-37 through -1	1 through 13
447	-26 through 25	-26 through -1	1 through 25
448	-30 through 212	-30 through -1	1 through 212
449	-60 through 94	-60 through -1	1 through 94
450	-61 through 28	-61 through -1	1 through 28
451	-26 through 47	-26 through -1	1 through 47
452	-34 through 20	-34 through -1	1 through 20
453	-38 through 83	-38 through -1	1 through 83
454	-37 through 129	-37 through -1	1 through 129
455	-26 through 154	-26 through -1	1 through 154
456	-64 through 27	-64 through -1	1 through 27
457	-23 through 234	-23 through -1	1 through 234
458	-60 through 133	-60 through -1	1 through 133
459	-28 through 79	-28 through -1	1 through 79
460	-13 through 108	-13 through -1	1 through 108
461	-17 through 27	-17 through -1	1 through 27
462	-13 through 96	-13 through -1	1 through 96
463	-41 through 102	-41 through -1	1 through 102
464	-30 through 202	-30 through -1	1 through 202
465	-21 through 40	-21 through -1	1 through 40
466	-19 through 15	-19 through -1	1 through 15
467	-54 through 161	-54 through -1	1 through 161
468	-17 through 10	-17 through -1	1 through 10
469	-24 through 61	-24 through -1	1 through 61
470	-16 through 35	-16 through -1	1 through 35
471	-43 through 24	-43 through -1	1 through 24
472	-15 through 48	-15 through -1	1 through 48
473	-58 through 121	-58 through -1	1 through 121
474	-71 through 167	-71 through -1	1 through 167
475	-37 through 141	-37 through -1	1 through 141
476	-21 through 75	-21 through -1	1 through 75
477	-24 through 17	-24 through -1	1 through 17
478	-27 through 86	-27 through -1	1 through 86
479	-18 through 232	-18 through -1	1 through 232
480	-21 through 130	-21 through -1	1 through 130
481	-25 through 214	-25 through -1	1 through 214
482	-92 through 116	-92 through -1	1 through 116
483	-39 through 47	-39 through -1	1 through 47
484	-27 through 13	-27 through -1	1 through 13
485	-16 through 49	-16 through -1	1 through 49
486	-55 through 75	-55 through -1	1 through 75
487	-84 through 125	-84 through -1	1 through 125
488	-17 through 19	-17 through -1	1 through 19
489	-29 through 15	-29 through -1	1 through 15

490	-52 through 111	-52 through -1	1 through 111
491	-47 through 17	-47 through -1	1 through 17
492	-50 through 168	-50 through -1	1 through 168
493	-15 through 201	-15 through -1	1 through 201
494	-19 through 115	-19 through -1	1 through 115
495	-16 through 69	-16 through -1	1 through 69
496	-29 through 263	-29 through -1	1 through 263
497	-56 through 66	-56 through -1	1 through 66
498	-28 through 31	-28 through -1	1 through 31
499	-13 through 86	-13 through -1	1 through 86
500	-13 through 86	-13 through -1	1 through 86
501	-25 through 83	-25 through -1	1 through 83
502	-15 through 168	-15 through -1	1 through 168
503	-15 through 83	-15 through -1	1 through 83
504	-57 through 126	-57 through -1	1 through 126
505	-14 through 126	-14 through -1	1 through 126
506	-14 through 45	-14 through -1	1 through 45
507	-36 through 65	-36 through -1	1 through 65
508	-55 through 286	-55 through -1	1 through 286
509	-42 through 66	-42 through -1	1 through 66
510	-26 through 54	-26 through -1	1 through 54
511	-44 through 114	-44 through -1	1 through 114
512	-28 through 102	-28 through -1	1 through 102
513	-62 through 137	-62 through -1	1 through 137
514	-25 through 155	-25 through -1	1 through 155

TABLE VI

Id	Collection refs	Deposit Name
40	ATCC # 98921	SignalTag 121-144
41	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
42	ATCC # 98921	SignalTag 121-144
43	ATCC # 98920	SignalTag 67-90
44	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
45	ATCC # 98920	SignalTag 67-90
46	ATCC # 98923	SignalTag 44-66
47	ATCC # 98920	SignalTag 67-90
48	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
49	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
50	ATCC # 98921	SignalTag 121-144
51	ATCC # 98921	SignalTag 121-144
52	ATCC # 98920	SignalTag 67-90
53	ATCC # 98923	SignalTag 44-66
54	ATCC # 98920	SignalTag 67-90
55	ATCC # 98920	SignalTag 67-90
56	ATCC # 98920	SignalTag 67-90
57	ATCC # 98921	SignalTag 121-144
58	ATCC # 98920	SignalTag 67-90
59	ATCC # 98920	SignalTag 67-90
60	ATCC # 98920	SignalTag 67-90
61	ATCC # 98923	SignalTag 44-66
62	ATCC # 98923	SignalTag 44-66
63	ATCC # 98923	SignalTag 44-66
64	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
65	ATCC # 98923	SignalTag 44-66
66	ATCC # 98921	SignalTag 121-144
67	ATCC # 98920	SignalTag 67-90
68	ATCC # 98920	SignalTag 67-90
69	ATCC # 98921	SignalTag 121-144
70	ATCC # 98921	SignalTag 121-144
71	ATCC # 98921	SignalTag 121-144
72	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
73	ATCC # 98923	SignalTag 44-66

74	ATCC # 98923	SignalTag 44-66
75	ATCC # 98920	SignalTag 67-90
76	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
77	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
78	ATCC # 98921	SignalTag 121-144
79	ATCC # 98923	SignalTag 44-66
80	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
81	ATCC # 98921	SignalTag 121-144
82	ATCC # 98920	SignalTag 67-90
83	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
84	ATCC # 98923	SignalTag 44-66
85	ATCC # 98923	SignalTag 44-66
86	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
87	ATCC # 98923	SignalTag 44-66
88	ATCC # 98923	SignalTag 44-66
89	ATCC # 98923	SignalTag 44-66
90	ATCC # 98923	SignalTag 44-66
91	ATCC # 98923	SignalTag 44-66
92	ATCC # 98920	SignalTag 67-90
93	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
94	ATCC # 98923	SignalTag 44-66
95	ATCC # 98923	SignalTag 44-66
96	ATCC # 98920	SignalTag 67-90
97	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
98	ATCC # 98921	SignalTag 121-144
99	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
100	ATCC # 98921	SignalTag 121-144
101	ATCC # 98920	SignalTag 67-90
102	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
103	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
104	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
105	ATCC # 98921	SignalTag 121-144
106	ATCC # 98920	SignalTag 67-90
107	ATCC # 98920	SignalTag 67-90
108	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
109	ATCC # 98923	SignalTag 44-66
110	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120

111	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
112	ATCC # 98920	SignalTag 67-90
113	ATCC # 98920	SignalTag 67-90
114	ATCC # 98923	SignalTag 44-66
115	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
116	ATCC # 98920	SignalTag 67-90
117	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
118	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
119	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
120	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
121	ATCC # 98923	SignalTag 44-66
122	ATCC # 98920	SignalTag 67-90
123	ATCC # 98920	SignalTag 67-90
124	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
125	ECACC # 98121506	SignalTag 11121998
126	ECACC # 98121506	SignalTag 11121998
127	ECACC # 98121506	SignalTag 11121998
128	ECACC # 98121506	SignalTag 11121998
129	ECACC # 98121506	SignalTag 11121998
130	ECACC # 98121506	SignalTag 11121998
131	ECACC # 98121506	SignalTag 11121998
132	ECACC # 98121506	SignalTag 11121998
133	ECACC # 98121506	SignalTag 11121998
134	ECACC # 98121506	SignalTag 11121998
135	ECACC # 98121506	SignalTag 11121998
136	ECACC # 98121506	SignalTag 11121998
137	ECACC # 98121506	SignalTag 11121998
138	ECACC # 98121506	SignalTag 11121998
139	ECACC # 98121506	SignalTag 11121998
140	ECACC # 98121506	SignalTag 11121998

TABLE VII

Internal designation number	SEQ ID NO	Type of sequence
20-5-2-C3-CL0_4	40	DNA
20-8-4-A11-CL2_6	41	DNA
21-1-4-F2-CL11_1	42	DNA
22-11-2-H9-CL1_1	43	DNA
25-7-3-D4-CL0_2	44	DNA
26-27-3-D7-CL0_1	45	DNA
26-35-4-H9-CL1_1	46	DNA
26-45-2-C4-CL2_6	47	DNA
27-1-2-B3-CL0_1	48	DNA
27-1-2-B3-CL0_2	49	DNA
27-19-3-G7-CL11_2	50	DNA
33-10-4-E2-CL13_4	51	DNA
33-10-4-H2-CL2_2	52	DNA
33-110-4-A5-CL1_1	53	DNA
33-13-1-C1-CL1_1	54	DNA
33-30-2-A6-CL0_1	55	DNA
33-35-4-F4-CL1_2	56	DNA
33-35-4-G1-CL1_2	57	DNA
33-36-3-E2-CL1_1	58	DNA
33-36-3-E2-CL1_2	59	DNA
33-36-3-F2-CL2_2	60	DNA
33-4-2-G5-CL2_1	61	DNA
33-49-1-H4-CL1_1	62	DNA
33-66-2-B10-CL4_1	63	DNA
33-97-4-G8-CL2_2	64	DNA
33-98-4-C1-CL1_3	65	DNA
47-14-1-C3-CL0_5	66	DNA
47-15-1-E11-CL0_1	67	DNA
47-15-1-H8-CL0_2	68	DNA
48-1-1-H7-CL0_1	69	DNA
48-1-1-H7-CL0_4	70	DNA
48-1-1-H7-CL0_5	71	DNA
48-3-1-H9-CL0_6	72	DNA
48-54-1-G9-CL2_1	73	DNA

48-54-1-G9-CL3_1	74	DNA
48-7-4-H2-CL2_2	75	DNA
51-11-3-D5-CL1_3	76	DNA
51-11-3-G9-CL0_1	77	DNA
51-15-4-A12-CL11_3	78	DNA
51-17-4-A4-CL3_1	79	DNA
51-2-3-F10-CL1_5	80	DNA
51-2-4-F5-CL11_2	81	DNA
51-27-4-F2-CL0_2	82	DNA
51-34-3-F8-CL0_2	83	DNA
57-1-4-E2-CL1_2	84	DNA
57-19-2-G8-CL2_1	85	DNA
57-27-3-G10-CL2_2	86	DNA
58-33-3-B4-CL1_2	87	DNA
58-34-3-C9-CL1_2	88	DNA
58-4-4-G2-CL2_1	89	DNA
58-48-1-G3-CL2_4	90	DNA
58-6-1-H4-CL1_1	91	DNA
60-12-1-E11-CL1_2	92	DNA
65-4-4-H3-CL1_1	93	DNA
74-5-1-E4-CL1_2	94	DNA
76-13-3-A9-CL1_2	95	DNA
76-16-1-D6-CL1_1	96	DNA
76-28-3-A12-CL1_5	97	DNA
76-42-2-F3-CL0_1	98	DNA
77-16-4-G3-CL1_3	99	DNA
77-39-4-H4-CL11_4	100	DNA
78-24-3-H4-CL2_1	101	DNA
78-27-3-D1-CL1_6	102	DNA
78-28-3-D2-CL0_2	103	DNA
78-7-1-G5-CL2_6	104	DNA
84-3-1-G10-CL11_6	105	DNA
58-48-4-E2-CL0_1	106	DNA
23-12-2-G6-CL1_2	107	DNA
25-8-4-B12-CL0_5	108	DNA
26-44-3-C5-CL2_1	109	DNA
27-1-2-B3-CL0_3	110	DNA

30-12-3-G5-CL0_1	111	DNA
33-106-2-F10-CL1_3	112	DNA
33-28-4-D1-CL0_1	113	DNA
33-31-3-C8-CL2_1	114	DNA
48-24-1-D2-CL3_2	115	DNA
48-46-4-A11-CL1_4	116	DNA
51-1-4-C1-CL0_2	117	DNA
51-39-3-H2-CL1_2	118	DNA
51-42-3-F9-CL1_1	119	DNA
51-5-3-G2-CL0_4	120	DNA
57-18-4-H5-CL2_1	121	DNA
76-23-3-G8-CL1_1	122	DNA
76-23-3-G8-CL1_3	123	DNA
78-8-3-E6-CL0_1	124	DNA
19-10-1-C2-CL1_3	125	DNA
33-11-1-B11-CL1_2	126	DNA
33-113-2-B8-CL1_2	127	DNA
33-19-1-C11-CL1_1	128	DNA
33-61-2-F6-CL0_2	129	DNA
47-4-4-C6-CL2_2	130	DNA
48-54-1-G9-CL1_1	131	DNA
51-43-3-G3-CL0_1	132	DNA
55-1-3-D11-CL0_1	133	DNA
58-14-2-D3-CL1_2	134	DNA
58-35-2-B6-CL2_3	135	DNA
76-18-1-F6-CL1_1	136	DNA
76-23-3-G8-CL2_2	137	DNA
76-30-3-B7-CL1_1	138	DNA
78-21-3-G7-CL2_1	139	DNA
58-45-4-B11-CL13_2	140	DNA
20-5-2-C3-CL0_4	141	PRT
20-8-4-A11-CL2_6	142	PRT
21-1-4-F2-CL11_1	143	PRT
22-11-2-H9-CL1_1	144	PRT
25-7-3-D4-CL0_2	145	PRT
26-27-3-D7-CL0_1	146	PRT
26-35-4-H9-CL1_1	147	PRT

26-45-2-C4-CL2_6	148	PRT
27-1-2-B3-CL0_1	149	PRT
27-1-2-B3-CL0_2	150	PRT
27-19-3-G7-CL11_2	151	PRT
33-10-4-E2-CL13_4	152	PRT
33-10-4-H2-CL2_2	153	PRT
33-110-4-A5-CL1_1	154	PRT
33-13-1-C1-CL1_1	155	PRT
33-30-2-A6-CL0_1	156	PRT
33-35-4-F4-CL1_2	157	PRT
33-35-4-G1-CL1_2	158	PRT
33-36-3-E2-CL1_1	159	PRT
33-36-3-E2-CL1_2	160	PRT
33-36-3-F2-CL2_2	161	PRT
33-4-2-G5-CL2_1	162	PRT
33-49-1-H4-CL1_1	163	PRT
33-66-2-B10-CL4_1	164	PRT
33-97-4-G8-CL2_2	165	PRT
33-98-4-C1-CL1_3	166	PRT
47-14-1-C3-CL0_5	167	PRT
47-15-1-E11-CL0_1	168	PRT
47-15-1-H8-CL0_2	169	PRT
48-1-1-H7-CL0_1	170	PRT
48-1-1-H7-CL0_4	171	PRT
48-1-1-H7-CL0_5	172	PRT
48-3-1-H9-CL0_6	173	PRT
48-54-1-G9-CL2_1	174	PRT
48-54-1-G9-CL3_1	175	PRT
48-7-4-H2-CL2_2	176	PRT
51-11-3-D5-CL1_3	177	PRT
51-11-3-G9-CL0_1	178	PRT
51-15-4-A12-CL11_3	179	PRT
51-17-4-A4-CL3_1	180	PRT
51-2-3-F10-CL1_5	181	PRT
51-2-4-F5-CL11_2	182	PRT
51-27-4-F2-CL0_2	183	PRT
51-34-3-F8-CL0_2	184	PRT

57-1-4-E2-CL1_2	185	PRT
57-19-2-G8-CL2_1	186	PRT
57-27-3-G10-CL2_2	187	PRT
58-33-3-B4-CL1_2	188	PRT
58-34-3-C9-CL1_2	189	PRT
58-4-4-G2-CL2_1	190	PRT
58-48-1-G3-CL2_4	191	PRT
58-6-1-H4-CL1_1	192	PRT
60-12-1-E11-CL1_2	193	PRT
65-4-4-H3-CL1_1	194	PRT
74-5-1-E4-CL1_2	195	PRT
76-13-3-A9-CL1_2	196	PRT
76-16-1-D6-CL1_1	197	PRT
76-28-3-A12-CL1_5	198	PRT
76-42-2-F3-CL0_1	199	PRT
77-16-4-G3-CL1_3	200	PRT
77-39-4-H4-CL11_4	201	PRT
78-24-3-H4-CL2_1	202	PRT
78-27-3-D1-CL1_6	203	PRT
78-28-3-D2-CL0_2	204	PRT
78-7-1-G5-CL2_6	205	PRT
84-3-1-G10-CL11_6	206	PRT
58-48-4-E2-CL0_1	207	PRT
23-12-2-G6-CL1_2	208	PRT
25-8-4-B12-CL0_5	209	PRT
26-44-3-C5-CL2_1	210	PRT
27-1-2-B3-CL0_3	211	PRT
30-12-3-G5-CL0_1	212	PRT
33-106-2-F10-CL1_3	213	PRT
33-28-4-D1-CL0_1	214	PRT
33-31-3-C8-CL2_1	215	PRT
48-24-1-D2-CL3_2	216	PRT
48-46-4-A11-CL1_4	217	PRT
51-1-4-C1-CL0_2	218	PRT
51-39-3-H2-CL1_2	219	PRT
51-42-3-F9-CL1_1	220	PRT
51-5-3-G2-CL0_4	221	PRT

57-18-4-H5-CL2_1	222	PRT
76-23-3-G8-CL1_1	223	PRT
76-23-3-G8-CL1_3	224	PRT
78-8-3-E6-CL0_1	225	PRT
19-10-1-C2-CL1_3	226	PRT
33-11-1-B11-CL1_2	227	PRT
33-113-2-B8-CL1_2	228	PRT
33-19-1-C11-CL1_1	229	PRT
33-61-2-F6-CL0_2	230	PRT
47-4-4-C6-CL2_2	231	PRT
48-54-1-G9-CL1_1	232	PRT
51-43-3-G3-CL0_1	233	PRT
55-1-3-D11-CL0_1	234	PRT
58-14-2-D3-CL1_2	235	PRT
58-35-2-B6-CL2_3	236	PRT
76-18-1-F6-CL1_1	237	PRT
76-23-3-G8-CL2_2	238	PRT
76-30-3-B7-CL1_1	239	PRT
78-21-3-G7-CL2_1	240	PRT
58-45-4-B11-CL13_2	241	PRT
20-6-1-D11-FL2	242	DNA
20-8-4-A11-FL2	243	DNA
22-6-2-C1-FL2	244	DNA
22-11-2-H9-FL1	245	DNA
23-8-3-B1-FL1	246	DNA
24-3-3-C6-FL1	247	DNA
24-4-1-H3-FL1	248	DNA
26-45-2-C4-FL2	249	DNA
26-48-1-H10-FL1	250	DNA
26-49-1-A5-FL2	251	DNA
30-6-4-E3-FL3	252	DNA
33-6-1-G11-FL1	253	DNA
33-8-1-A3-FL2	254	DNA
33-11-3-C6-FL1	255	DNA
33-14-4-E1-FL1	256	DNA
33-21-2-D5-FL1	257	DNA
33-26-4-E10-FL1	258	DNA

33-27-1-E11-FL1	259	DNA
33-28-4-D1-FL1	260	DNA
33-28-4-E2-FL2	261	DNA
33-30-4-C4-FL1	262	DNA
33-35-4-F4-FL1	263	DNA
33-36-3-F2-FL2	264	DNA
33-52-4-F9-FL2	265	DNA
33-52-4-H3-FL1	266	DNA
33-59-1-B7-FL1	267	DNA
33-71-1-A8-FL1	268	DNA
33-72-2-B2-FL1	269	DNA
33-105-2-C3-FL1	270	DNA
33-107-4-C3-FL1	271	DNA
33-110-2-G4-FL1	272	DNA
47-7-4-D2-FL2	273	DNA
47-10-2-G12-FL1	274	DNA
47-14-3-D8-FL1	275	DNA
47-18-3-C2-FL1	276	DNA
47-18-3-G5-FL2	277	DNA
47-18-4-E3-FL2	278	DNA
48-3-1-H9-FL3	279	DNA
48-4-2-H3-FL1	280	DNA
48-6-1-C9-FL1	281	DNA
48-7-4-H2-FL2	282	DNA
48-8-1-D8-FL3	283	DNA
48-13-3-H8-FL1	284	DNA
48-19-3-A7-FL1	285	DNA
48-19-3-G1-FL1	286	DNA
48-25-4-D8-FL1	287	DNA
48-21-4-H4-FL1	288	DNA
48-26-3-B8-FL2	289	DNA
48-29-1-E2-FL1	290	DNA
48-31-3-F7-FL1	291	DNA
48-47-3-A5-FL1	292	DNA
51-1-1-G12-FL1	293	DNA
51-1-4-E9-FL3	294	DNA
51-1-4-E9-FL2	295	DNA

51-2-1-E10-FL1	296	DNA
51-2-3-F10-FL1	297	DNA
51-2-4-F5-FL1	298	DNA
51-3-3-B10-FL2	299	DNA
51-3-3-B10-FL3	300	DNA
51-7-3-G3-FL1	301	DNA
51-10-3-D11-FL1	302	DNA
51-11-3-D5-FL1	303	DNA
51-13-1-F7-FL3	304	DNA
51-15-4-H10-FL1	305	DNA
51-17-4-A4-FL1	306	DNA
51-18-1-C3-FL1	307	DNA
51-25-3-F3-FL1	308	DNA
51-27-1-E8-FL1	309	DNA
51-28-2-G1-FL2	310	DNA
51-39-3-H2-FL1	311	DNA
51-42-3-F9-FL1	312	DNA
51-44-4-H4-FL1	313	DNA
55-1-3-H10-FL1	314	DNA
55-5-4-A6-FL1	315	DNA
58-26-3-D1-FL1	316	DNA
57-18-1-D5-FL1	317	DNA
57-27-3-A11-FL1	318	DNA
57-27-3-G10-FL2	319	DNA
58-10-3-D12-FL1	320	DNA
58-11-1-G10-FL1	321	DNA
58-11-2-G8-FL2	322	DNA
58-36-3-A9-FL2	323	DNA
58-38-1-A2-FL2	324	DNA
58-38-1-E5-FL1	325	DNA
58-44-2-B3-FL3	326	DNA
58-45-3-H11-FL1	327	DNA
58-53-2-B12-FL2	328	DNA
59-9-4-A10-FL1	329	DNA
60-16-3-A6-FL1	330	DNA
60-17-3-G8-FL2	331	DNA
62-5-4-B10-FL1	332	DNA

65-4-4-H3-FL1	333	DNA
74-3-1-B9-FL1	334	DNA
76-4-1-G5-FL1	335	DNA
76-7-3-A12-FL1	336	DNA
76-16-4-C9-FL3	337	DNA
76-30-3-B7-FL1	338	DNA
77-5-1-C2-FL1	339	DNA
77-5-4-E7-FL1	340	DNA
77-11-1-A3-FL1	341	DNA
77-16-3-D7-FL1	342	DNA
77-16-4-G3-FL1	343	DNA
77-25-1-A6-FL1	344	DNA
77-26-2-F2-FL3	345	DNA
78-6-2-E3-FL2	346	DNA
78-7-1-G5-FL2	347	DNA
78-16-2-C2-FL1	348	DNA
78-18-3-B4-FL3	349	DNA
78-20-1-G11-FL1	350	DNA
78-22-3-E10-FL1	351	DNA
78-24-2-B8-FL1	352	DNA
78-24-3-A8-FL1	353	DNA
78-24-3-H4-FL2	354	DNA
78-25-1-F11-FL1	355	DNA
78-26-1-B5-FL1	356	DNA
78-27-3-D1-FL1	357	DNA
78-29-1-B2-FL1	358	DNA
78-29-4-B6-FL1	359	DNA
14-1-3-E6-FL1	360	DNA
30-9-1-G8-FL2	361	DNA
33-10-4-H2-FL2	362	DNA
33-10-4-H2-FL1	363	DNA
74-10-3-C9-FL2	364	DNA
33-97-4-G8-FL3	365	DNA
33-97-4-G8-FL2	366	DNA
33-104-4-H4-FL1	367	DNA
47-2-3-B3-FL1	368	DNA
47-37-4-G11-FL1	369	DNA

57-25-1-F10-FL2	370	DNA
58-19-3-D3-FL1	371	DNA
58-34-3-C9-FL2	372	DNA
58-48-4-E2-FL2	373	DNA
76-21-1-C4-FL1	374	DNA
78-26-2-H7-FL1	375	DNA
77-20-2-E11-FL1	376	DNA
47-1-3-F7-FL2	377	DNA
20-6-1-D11-FL2	378	PRT
20-8-4-A11-FL2	379	PRT
22-6-2-C1-FL2	380	PRT
22-11-2-H9-FL1	381	PRT
23-8-3-B1-FL1	382	PRT
24-3-3-C6-FL1	383	PRT
24-4-1-H3-FL1	384	PRT
26-45-2-C4-FL2	385	PRT
26-48-1-H10-FL1	386	PRT
26-49-1-A5-FL2	387	PRT
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33-6-1-G11-FL1	389	PRT
33-8-1-A3-FL2	390	PRT
33-11-3-C6-FL1	391	PRT
33-14-4-E1-FL1	392	PRT
33-21-2-D5-FL1	393	PRT
33-26-4-E10-FL1	394	PRT
33-27-1-E11-FL1	395	PRT
33-28-4-D1-FL1	396	PRT
33-28-4-E2-FL2	397	PRT
33-30-4-C4-FL1	398	PRT
33-35-4-F4-FL1	399	PRT
33-36-3-F2-FL2	400	PRT
33-52-4-F9-FL2	401	PRT
33-52-4-H3-FL1	402	PRT
33-59-1-B7-FL1	403	PRT
33-71-1-A8-FL1	404	PRT
33-72-2-B2-FL1	405	PRT
33-105-2-C3-FL1	406	PRT

33-107-4-C3-FL1	407	PRT
33-110-2-G4-FL1	408	PRT
47-7-4-D2-FL2	409	PRT
47-10-2-G12-FL1	410	PRT
47-14-3-D8-FL1	411	PRT
47-18-3-C2-FL1	412	PRT
47-18-3-G5-FL2	413	PRT
47-18-4-E3-FL2	414	PRT
48-3-1-H9-FL3	415	PRT
48-4-2-H3-FL1	416	PRT
48-6-1-C9-FL1	417	PRT
48-7-4-H2-FL2	418	PRT
48-8-1-D8-FL3	419	PRT
48-13-3-H8-FL1	420	PRT
48-19-3-A7-FL1	421	PRT
48-19-3-G1-FL1	422	PRT
48-25-4-D8-FL1	423	PRT
48-21-4-H4-FL1	424	PRT
48-26-3-B8-FL2	425	PRT
48-29-1-E2-FL1	426	PRT
48-31-3-F7-FL1	427	PRT
48-47-3-A5-FL1	428	PRT
51-1-1-G12-FL1	429	PRT
51-1-4-E9-FL3	430	PRT
51-1-4-E9-FL2	431	PRT
51-2-1-E10-FL1	432	PRT
51-2-3-F10-FL1	433	PRT
51-2-4-F5-FL1	434	PRT
51-3-3-B10-FL2	435	PRT
51-3-3-B10-FL3	436	PRT
51-7-3-G3-FL1	437	PRT
51-10-3-D11-FL1	438	PRT
51-11-3-D5-FL1	439	PRT
51-13-1-F7-FL3	440	PRT
51-15-4-H10-FL1	441	PRT
51-17-4-A4-FL1	442	PRT
51-18-1-C3-FL1	443	PRT

51-25-3-F3-FL1	444	PRT
51-27-1-E8-FL1	445	PRT
51-28-2-G1-FL2	446	PRT
51-39-3-H2-FL1	447	PRT
51-42-3-F9-FL1	448	PRT
51-44-4-H4-FL1	449	PRT
55-1-3-H10-FL1	450	PRT
55-5-4-A6-FL1	451	PRT
58-26-3-D1-FL1	452	PRT
57-18-1-D5-FL1	453	PRT
57-27-3-A11-FL1	454	PRT
57-27-3-G10-FL2	455	PRT
58-10-3-D12-FL1	456	PRT
58-11-1-G10-FL1	457	PRT
58-11-2-G8-FL2	458	PRT
58-36-3-A9-FL2	459	PRT
58-38-1-A2-FL2	460	PRT
58-38-1-E5-FL1	461	PRT
58-44-2-B3-FL3	462	PRT
58-45-3-H11-FL1	463	PRT
58-53-2-B12-FL2	464	PRT
59-9-4-A10-FL1	465	PRT
60-16-3-A6-FL1	466	PRT
60-17-3-G8-FL2	467	PRT
62-5-4-B10-FL1	468	PRT
65-4-4-H3-FL1	469	PRT
74-3-1-B9-FL1	470	PRT
76-4-1-G5-FL1	471	PRT
76-7-3-A12-FL1	472	PRT
76-16-4-C9-FL3	473	PRT
76-30-3-B7-FL1	474	PRT
77-5-1-C2-FL1	475	PRT
77-5-4-E7-FL1	476	PRT
77-11-1-A3-FL1	477	PRT
77-16-3-D7-FL1	478	PRT
77-16-4-G3-FL1	479	PRT
77-25-1-A6-FL1	480	PRT

77-26-2-F2-FL3	481	PRT
78-6-2-E3-FL2	482	PRT
78-7-1-G5-FL2	483	PRT
78-16-2-C2-FL1	484	PRT
78-18-3-B4-FL3	485	PRT
78-20-1-G11-FL1	486	PRT
78-22-3-E10-FL1	487	PRT
78-24-2-B8-FL1	488	PRT
78-24-3-A8-FL1	489	PRT
78-24-3-H4-FL2	490	PRT
78-25-1-F11-FL1	491	PRT
78-26-1-B5-FL1	492	PRT
78-27-3-D1-FL1	493	PRT
78-29-1-B2-FL1	494	PRT
78-29-4-B6-FL1	495	PRT
14-1-3-E6-FL1	496	PRT
30-9-1-G8-FL2	497	PRT
33-10-4-H2-FL2	498	PRT
33-10-4-H2-FL1	499	PRT
74-10-3-C9-FL2	500	PRT
33-97-4-G8-FL3	501	PRT
33-97-4-G8-FL2	502	PRT
33-104-4-H4-FL1	503	PRT
47-2-3-B3-FL1	504	PRT
47-37-4-G11-FL1	505	PRT
57-25-1-F10-FL2	506	PRT
58-19-3-D3-FL1	507	PRT
58-34-3-C9-FL2	508	PRT
58-48-4-E2-FL2	509	PRT
76-21-1-C4-FL1	510	PRT
78-26-2-H7-FL1	511	PRT
77-20-2-E11-FL1	512	PRT
47-1-3-F7-FL2	513	PRT

TABLE VIII

ID	Locations	PROSITE Signature Name
195	110-121	Aldehyde dehydrogenases csyteine active site
221	28-37	ATP synthase alpha and beta subunits signature
223	171-181	Regulator of chromosome condensation (RCC1) signature 2
225	90-112	Phosphatidylethanolamine-binding protein family signature
226	10-34	Protein kinases ATP-binding region signature

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto.

2. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto.

3. A purified or isolated nucleic acid comprising the full coding sequences of one of SEQ ID NOs: 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein.

4. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.

5. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide.

6. A purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

7. A purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

8. A purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

9. A purified or isolated protein comprising the sequence of one of SEQ ID NOs: 141-241 and 378-513.

10. A purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

11. An isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

12. An isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

13. A method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of:

obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-377; inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter; and introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA.

14. The method of Claim 13, further comprising the step of isolating said protein.

15. A protein obtainable by the method of Claim 14.

16. A host cell containing a recombinant nucleic acid of Claim 1.

17. A purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513.

18. In an array of polynucleotides of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides.

19. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEQ ID NOs: 40-140 and 242-377.

20. A purified or isolated antibody capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

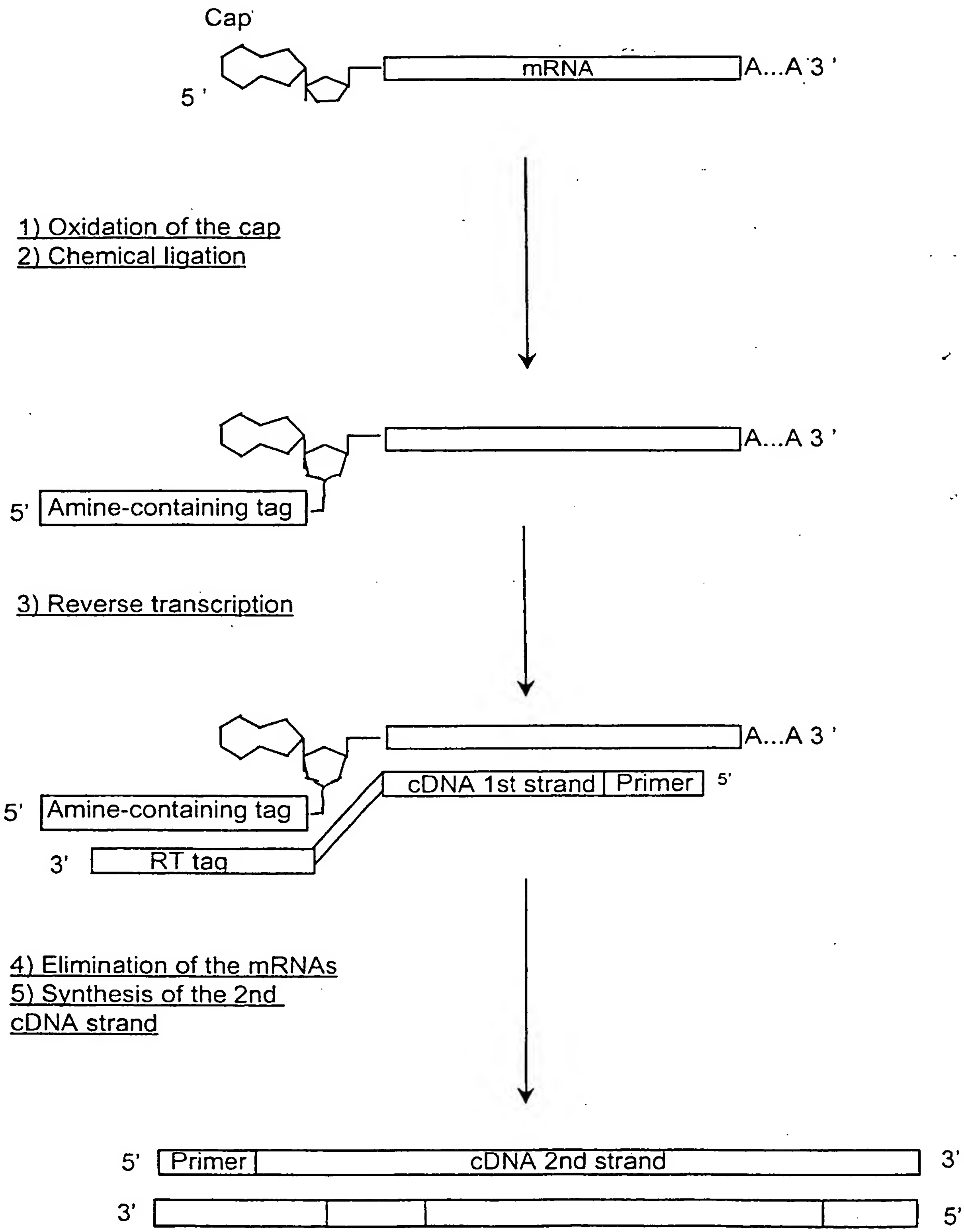

Cap
5 '
mRNA
A...A 3 '
1) Oxidation of the cap
2) Chemical ligation
A...A 3 '
5' Amine-containing tag
3) Reverse transcription
A...A 3 '
cDNA 1st strand
Primer
5'
5' Amine-containing tag
3' RT tag
4) Elimination of the mRNAs
5) Synthesis of the 2nd cDNA strand
5' Primer cDNA 2nd strand 3'
3' 5'

Figure 1

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
3,5	0,121	0,036	0,467	0,664
4	0,096	0,06	0,519	0,708
4,5	0,078	0,079	0,565	0,745
5	0,062	0,098	0,615	0,782
5,5	0,05	0,127	0,659	0,813
6	0,04	0,163	0,694	0,836
6,5	0,033	0,202	0,725	0,855
7	0,025	0,248	0,763	0,878
7,5	0,021	0,304	0,78	0,889
8	0,015	0,368	0,816	0,909
8,5	0,012	0,418	0,836	0,92
9	0,009	0,512	0,856	0,93
9,5	0,007	0,581	0,863	0,934
10	0,006	0,679	0,835	0,919

FIGURE 2

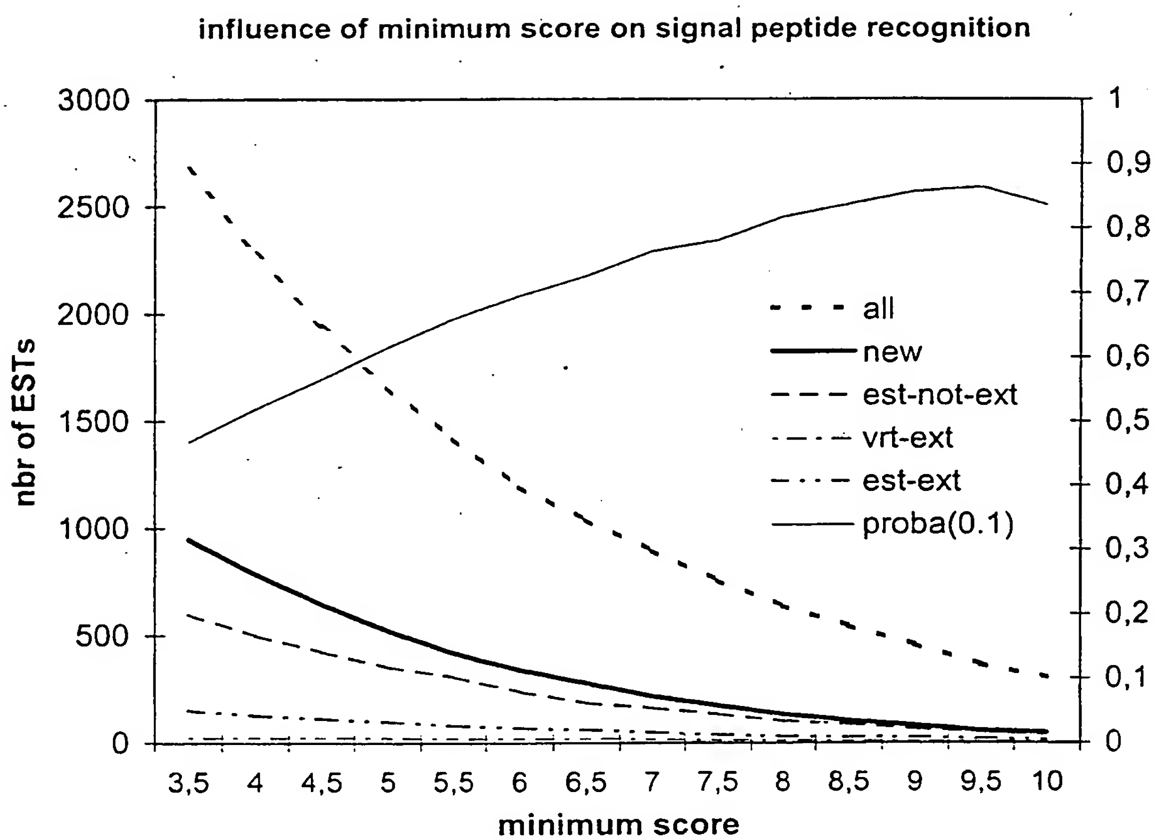

influence of minimum score on signal peptide recognition
nbr of ESTs
3000
2500
2000
1500
1000
500
0
1
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
all
new
est-not-ext
vrt-ext
est-ext
proba(0.1)
3,5
4
4,5
5
5,5
6
6,5
7
7,5
8
8,5
9
9,5
10
minimum score

FIGURE 3

Minimum signal peptide score	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
3,5	2674	947	599	23	150
4	2278	784	499	23	126
4,5	1943	647	425	22	112
5	1657	523	353	21	96
5,5	1417	419	307	19	80
6	1190	340	238	18	68
6,5	1035	280	186	18	60
7	893	219	161	15	48
7,5	753	173	132	12	36
8	636	133	101	11	29
8,5	543	104	83	8	26
9	456	81	63	6	24
9,5	364	57	48	6	18
10	303	47	35	6	15

FIGURE 4

Tissue	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
Brain	329	131	75	3	24
Cancerous prostate	134	40	37	1	6
Cerebellum	17	9	1	0	6
Colon	21	11	4	0	0
Dystrophic muscle	41	18	8	0	1
Fetal brain	70	37	16	0	1
Fetal kidney	227	116	46	1	19
Fetal liver	13	7	2	0	0
Heart	30	15	7	0	1
Hypertrophic prostate	86	23	22	2	2
Kidney	10	7	3	0	0
Large intestine	21	8	4	0	1
Liver	23	9	6	0	0
Lung	24	12	4	0	1
Lung (cells)	57	38	6	0	4
Lymph ganglia	163	60	23	2	12
Lymphocytes	23	6	4	0	2
Muscle	33	16	6	0	4
Normal prostate	181	61	45	7	11
Ovary	90	57	12	1	2
Pancreas	48	11	6	0	1
Placenta	24	5	1	0	0
Prostate	34	16	4	0	2
Spleen	56	28	10	0	1
Substantia nigra	108	47	27	1	6
Surrenals	15	3	3	1	0
Testis	131	68	25	1	8
Thyroid	17	8	2	0	2
Umbilical cord	55	17	12	1	3
Uterus	28	15	3	0	2
Non tissue-specific	568	48	177	2	28
Total	2677	947	601	23	150

FIGURE 5

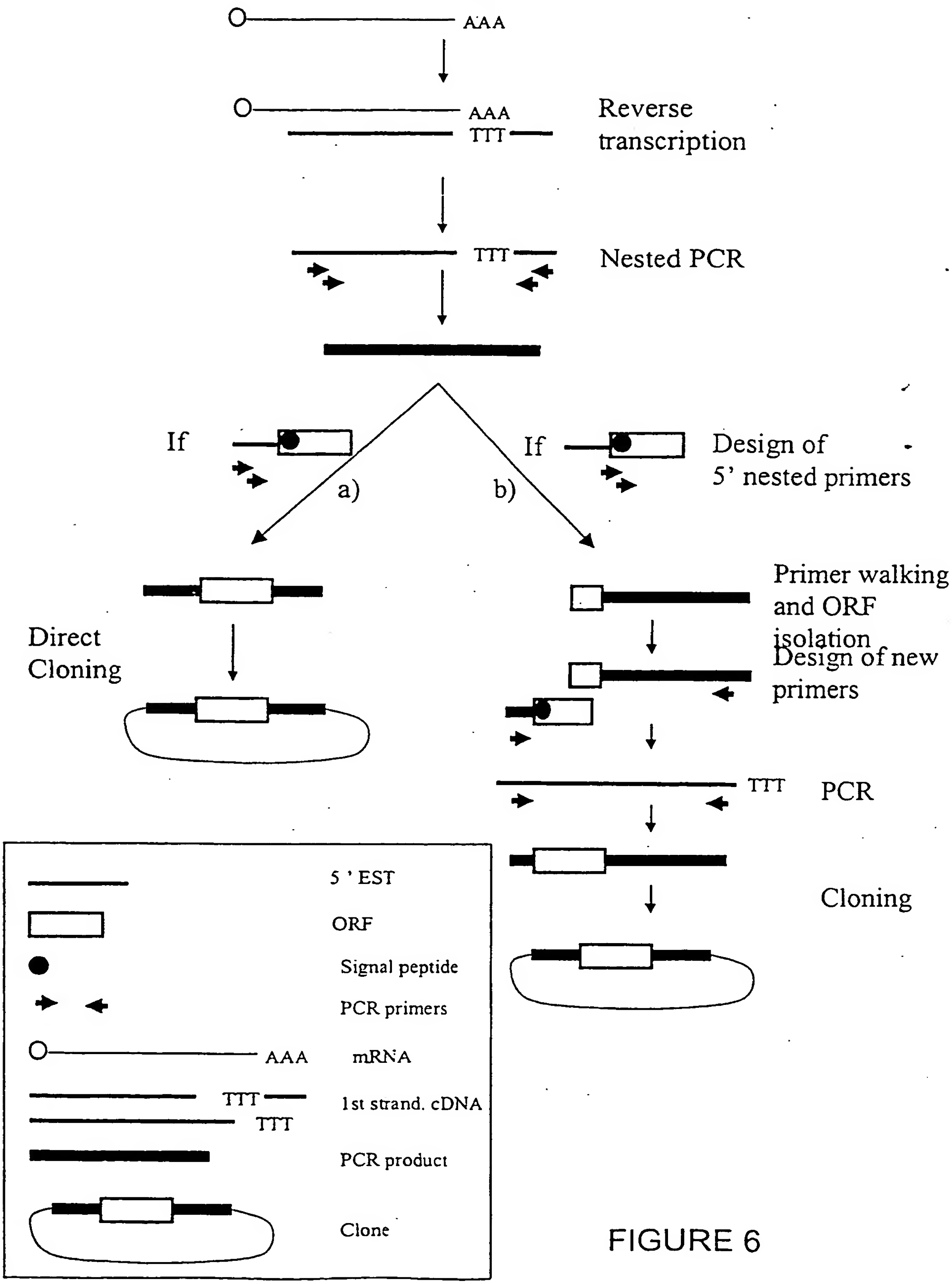
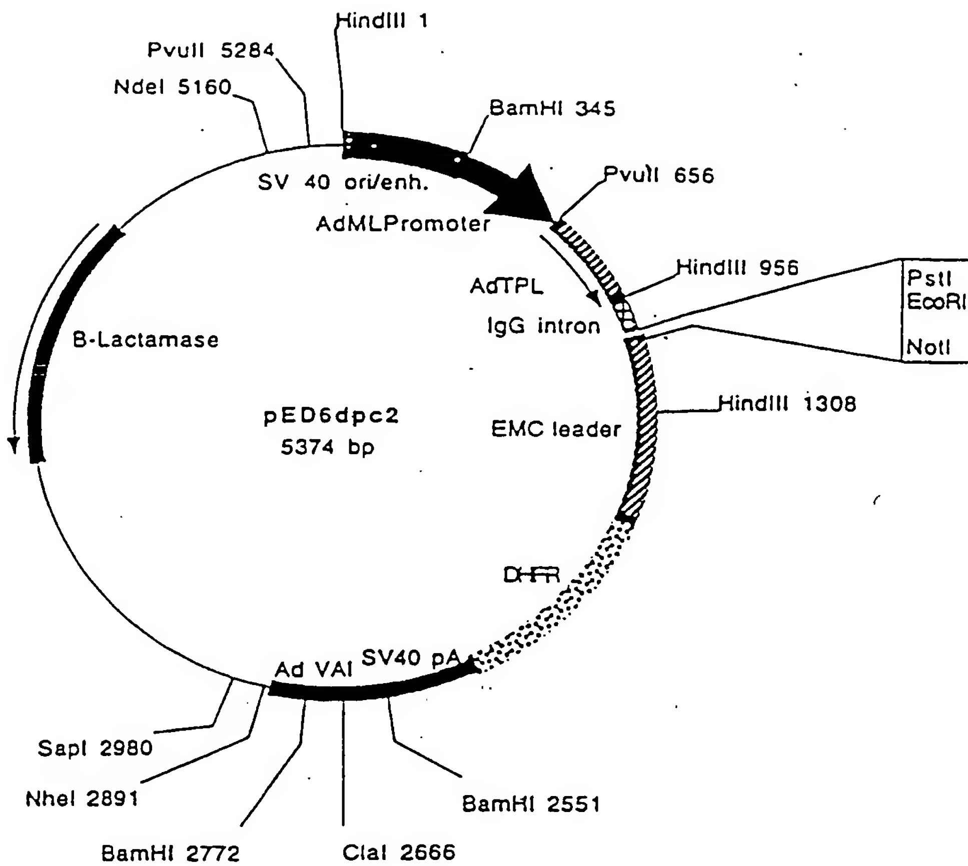

AAA
AAA
TTT
Reverse transcription
TTT
Nested PCR
If
If
a)
b)
Design of 5' nested primers
Primer walking and ORF isolation
Design of new primers
Direct Cloning
TTT
PCR
Cloning
5 ' EST
ORF
Signal peptide
PCR primers
AAA
mRNA
TTT
TTT
1st strand. cDNA
PCR product
Clone

FIGURE 6



Plasmid name: pED6dpc2
Plasmid size: 5374 bp

FIGURE 7

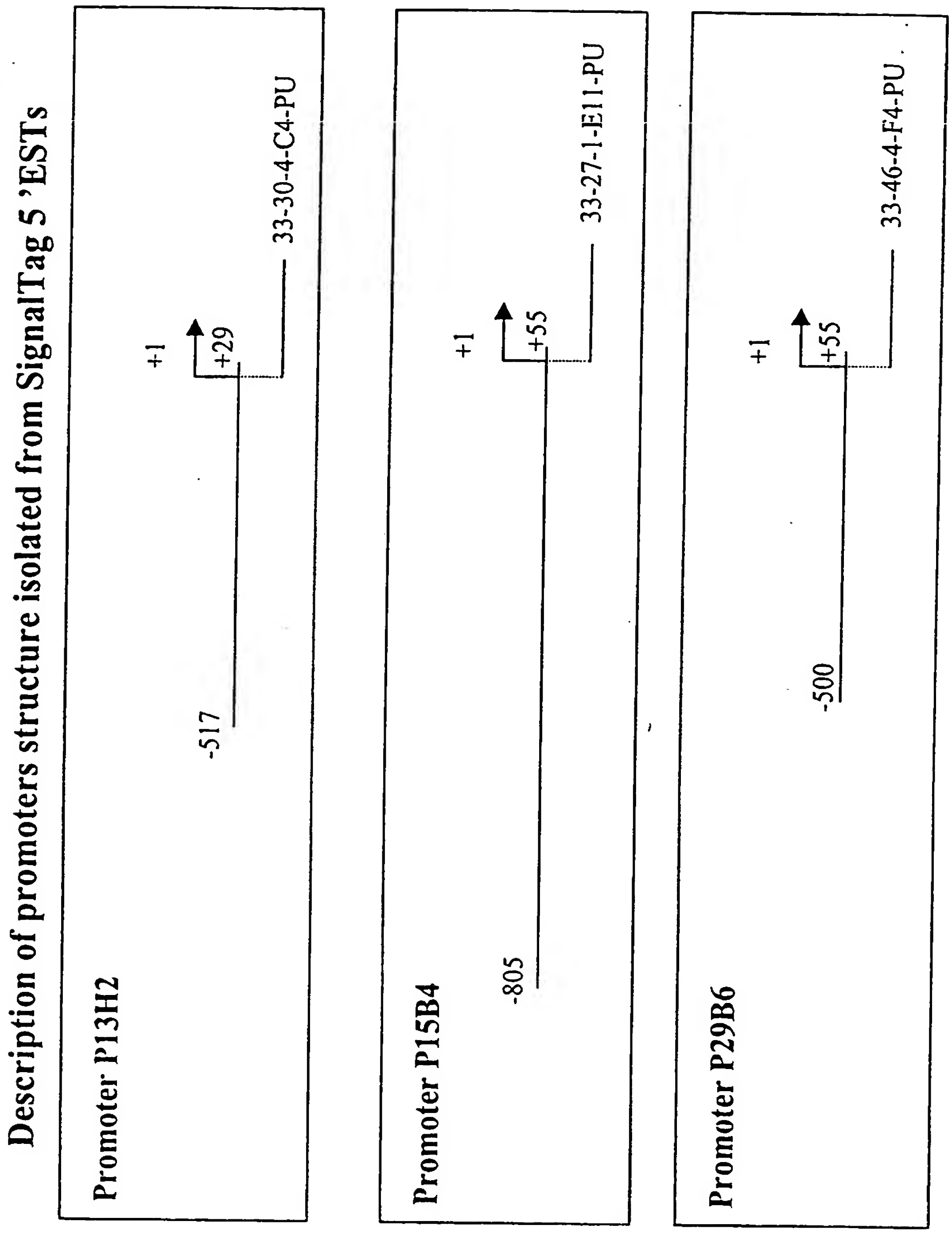

Description of promoters structure isolated from SignalTag 5 'ESTs
Promoter P13H2
-517
+1
+29
33-30-4-C4-PU
Promoter P15B4
-805
+1
+55
33-27-1-E11-PU
Promoter P29B6
-500
+1
+55
33-46-4-F4-PU

FIGURE 8

Description of Transcription Factor Binding Sites present on promoters isolated from SignalTag sequences

Promoter sequence P13H2 (546 bp):

Matrix	Position	Orientation	Score	Length	Sequence
CMYB_01	-502	+	0.983	9	TGTCAGTTG
MYOD_Q6	-501	-	0.961	10	CCCAACTGAC
S8_01	-444	-	0.960	11	AATAGAATTAG
S8_01	-425	+	0.966	11	AACTAAATTAG
DELTAEF1_01	-390	-	0.960	11	GCACACCTCAG
GATA_C	-364	-	0.964	11	AGATAAATCCA
CMYB_01	-349	+	0.958	9	CTTCAGTTG
GATA1_02	-343	+	0.959	14	TTGTAGATAGGACA
GATA_C	-339	+	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	+	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	+	0.983	16	CATAACAGATGGTAAG
TAL1BETAITF2_01	-235	+	0.978	16	CATAACAGATGGTAAG
MYOD_Q6	-232	-	0.954	10	ACCATCTGTT
GATA1_04	-217	-	0.953	13	TCAAGATAAAGTA
IK1_01	-126	+	0.963	13	AGTTGGGAATTCC
IK2_01	-126	+	0.985	12	AGTTGGGAATTC
CREL_01	-123	+	0.962	10	TGGGAATTCC
GATA1_02	-96	+	0.950	14	TCAGTGATATGGCA
SRY_02	-41	-	0.951	12	TAAAACAAAACA
E2F_02	-33	+	0.957	8	TTTAGCGC
MZF1_01	-5	-	0.975	8	TGAGGGGA

Promoter sequence P15B4 (861bp) :

Matrix	Position	Orientation	Score	Length	Sequence
NFY_Q6	-748	-	0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	+	0.994	9	TGACCGTTG
VMYB_02	-682	-	0.985	9	TCCAACGGT
STAT_01	-673	+	0.968	9	TTCCTGGAA
STAT_01	-673	-	0.951	9	TTCCAGGAA
MZF1_01	-556	-	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	+	0.986	8	AGAGGGGA
SRY_02	-398	-	0.955	12	GAAAACAAAACA
MZF1_01	-216	+	0.960	8	GAAGGGGA
MYOD_Q6	-190	+	0.981	10	AGCATCTGCC
DELTAEF1_01	-176	+	0.958	11	TCCCACCTTCC
S8_01	5	-	0.992	11	GAGGCAATTAT
MZF1_01	16	-	0.986	8	AGAGGGGA

Promoter sequence P29B6 (555 bp) :

Matrix	Position	Orientation	Score	Length	Sequence
ARNT_01	-311	+	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	+	0.965	12	ACTCACGTGCTG
USF_01	-309	+	0.985	12	ACTCACGTGCTG
USF_01	-309	-	0.985	12	CAGCACGTGAGT
NMYC_01	-309	-	0.956	12	CAGCACGTGAGT
MYCMAX_02	-309	-	0.972	12	CAGCACGTGAGT
USF_C	-307	+	0.997	8	TCACGTGC
USF_C	-307	-	0.991	8	GCACGTGA
MZF1_01	-292	-	0.968	8	CATGGGGA
ELK1_02	-105	+	0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10	TCCGGAAGCC
AP1_Q4	-42	-	0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42	-	0.961	11	AGTGACTGAAC
PADS_C	45	+	1.000	9	TGTGGTCTC

Figure 9

```
100.0% identity in 125 aa overlap

                            10        20        30        40        50        60
SEQ ID NO: 217 MADEELEALRRQRLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA
               X:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO: 516 MADEELEALRRQRLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA
                            10        20        30        40        50        60

                            70        80        90       100       110       120
SEQ ID NO: 217 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD
               ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO: 516 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD
                            70        80        90       100       110       120

SEQ ID NO: 217 EDDDY
               ::::X
SEQ ID NO: 516 EDDDY

----------
```

FIGURE 10

```
CLUSTAL W(1.5) multiple sequence alignment


SEQ ID NO: 517      MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLS
SEQ ID NO: 232      ---------------------------------------MGCVFQSTEDKCIFKIDWTLS
SEQ ID NO: 174      ---------------------------------------MGCVFQSTEDKRIFKIDWTLS
SEQ ID NO: 175      ---------------------------------------MGCVFQSTVDKCIFKIDWTLS
                                                           ******** ** *********

SEQ ID NO: 517      PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQDVE----------
SEQ ID NO: 232      PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL
SEQ ID NO: 174      PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQEADQGTYICEIRL
SEQ ID NO: 175      PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL
                    ********************************* *************. .

SEQ ID NO: 517      ------------------------------------------------------------
SEQ ID NO: 232      KGESQVFKKAVVLHVLPEEPKGTQMLT---------------------------------
SEQ ID NO: 174      KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEE
SEQ ID NO: 175      KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGR--RAK


SEQ ID NO: 517      ------------------------------------------------------------
SEQ ID NO: 232      ------------------------------------------------------------
SEQ ID NO: 174      IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN
SEQ ID NO: 175      VTRRKHHCVREGSG----------------------------------------------


SEQ ID NO: 517      ------------------------------------------------------------
SEQ ID NO: 232      ------------------------------------------------------------
SEQ ID NO: 174      LVFKKTIVLHVSPEEPRTLVTPAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKTC
SEQ ID NO: 175      ------------------------------------------------------------


SEQ ID NO: 517      --------------------
SEQ ID NO: 232      --------------------
SEQ ID NO: 174      GNKSSVNSTVLVKNTKKTNP
SEQ ID NO: 175      --------------------
```

FIGURE 11

99.6% identity in 225 aa overlap

```
                10        20        30        40        50        60
SEQ ID NO: 515  PTAVQKEEARQDVEALLSRTVRTQILTGKELRVATQEKEGSSGRCMLTLLGLSFILAGLI
                                              ::::::::::::::::::::::::::::::
SEQ ID NO: 231                                LRVATQEKEGSSGRCMLTLLGLSFILAGLI
                                                      10        20        30

                70        80        90        100       110       120
SEQ ID NO: 515  VGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIAIIDV
                ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO: 231  VGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIAIIDV
                        40        50        60        70        80        90

                130       140       150       160       170       180
SEQ ID NO: 515  PVPSFSDSDPAAIIHDFEKGMTAYLDLLLGNCYLMPLNTSIVMPPKNLVELFGKLASGRY
                :::::::::::::::::::::::::::::: :::::::::::::::::::::::::::::
SEQ ID NO: 231  PVPSFSDSDPAAIIHDFEKGMTAYLDLLLGICYLMPLNTSIVMPPKNLVELFGKLASGRY
                        100       110       120       130       140       150

                190       200       210       220       230       240
SEQ ID NO: 515  LPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR
                ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO: 231  LPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR
                        160       170       180       190       200       210

                250       260
SEQ ID NO: 515  HFPNEFIVETKICQE
                :::::::::::::::
SEQ ID NO: 231  HFPNEFIVETKICQE
                       220
```

FIGURE 12

```
99.7% identity in 353 aa overlap

                                                    10        20        30
SEQ ID NO:196                               MERGLKSADPRDGTGYTGWAGIAVLYLHLY
                                            ::::::::::::::::::::::::::::::
SEQ ID NO:518 LAEGYFDAAGRLTPEFSQRLTNKIRELLQQMERGLKSADPRDGTGYTGWAGIAVLYLHLY
                20        30        40        50        60        70

                      40        50        60        70        80        90
SEQ ID NO:196 DVFGDPAYLQLAHGYVKQSLNCLTKRSITFLCGDAGPLAVAAVLYHKMNNEKQAEDCITR
              ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO:518 DVFGDPAYLQLAHGYVKQSLNCLTKRSITFLCGDAGPLAVAAVLYHKMNNEKQAEDCITR
                80        90       100       110       120       130

                     100       110       120       130       140       150
SEQ ID NO:196 LIHLNKIDPHAPNEMLYGRIGYIYALLFVNKNFGVEKTPQSHIQQICETILTSGENLARK
              :::::::::::::::::::::::::::::::::::::.::::::::::::::::::::::
SEQ ID NO:518 LIHLNKIDPHAPNEMLYGRIGYIYALLFVNKNFGVEKIPQSHIQQICETILTSGENLARK
               140       150       160       170       180       190

                     160       170       180       190       200       210
SEQ ID NO:196 RNFTAKSPLMYEWYQEYYVGAAHGLAGIYYYLMQPSLQVSQGKLHSLVKPSVDYVCQLKF
              ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO:518 RNFTAKSPLMYEWYQEYYVGAAHGLAGIYYYLMQPSLQVSQGKLHSLVKPSVDYVCQLKF
               200       210       220       230       240       250

                     220       230       240       250       260       270
SEQ ID NO:196 PSGNYPPCIGDNRDLLVHWCHGAPGVIYMLIQAYKVFREEKYLCDAYQCADVIWQYGLLK
              ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO:518 PSGNYPPCIGDNRDLLVHWCHGAPGVIYMLIQAYKVFREEKYLCDAYQCADVIWQYGLLK
               260       270       280       290       300       310

                     280       290       300       310       320       330
SEQ ID NO:196 KGYGLCHGSAGNAYAFLTLYNLTQDMKYLYRACKFAEWCLEYGEHGCRTPDTPFSLFEGM
              ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO:518 KGYGLCHGSAGNAYAFLTLYNLTQDMKYLYRACKFAEWCLEYGEHGCRTPDTPFSLFEGM
               320       330       340       350       360       370

                     340       350
SEQ ID NO:196 AGTIYFLADLLVPTKARFPAFEL
              :::::::::::::::::::::::
SEQ ID NO:518 AGTIYFLADLLVPTKARFPAFEL
               380       390
```

FIGURE 13

98.5% identity in 194 aa overlap

```
                       90        100       110       120       130       140
SEQ ID NO:519 ARNLPPLTDAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL
              ::::::::.:::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ ID NO:158 ARNLPPLTEAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL
                 60        70        80        90       100       110

                      150       160       170       180       190       200
SEQ ID NO:519 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIAQTLQEWCVGCEVVLSGIEEQVSRANQHKEQ
              ::::::::::::::::::::::::::::::.:::::::::::::::::::::::::::::
SEQ ID NO:158 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIARTLQEWCVGCEVVLSGIEEQVSRANQHKEQ
                120       130       140       150       160       170

                      210       220       230       240       250       260
SEQ ID NO:519 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPASGTNQRQPSKKASKG
              ::::::::::::::::::::::::::::::::::::::::::::.:::::::::::::::
SEQ ID NO:158 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPAPGTNQRQPSKKASKG
                180       190       200       210       220       230

                      270
SEQ ID NO:519 KGLRGSAKIWSKSN
              ::::::::::::::
SEQ ID NO:158 KGLRGSAKIWSKSN
                240       250
```

88.7% identity in 62 aa overlap

```
                       10        20        30        40        50        60
SEQ ID NO:519 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELAESDF
              :::::::::::::::::::::::::::::::::::::::::::::::::::::::.....
SEQ ID NO:158 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELXARNL
                       10        20        30        40        50        60

SEQ ID NO:519 AS
              .X
SEQ ID NO:158 PP
```

FIGURE 14

```
68.9% identity in 74 aa overlap

                         10        20        30        40        50
SEQ ID NO:226  MIARRNPVPLRFLPDEARSLPPPKLTDPRLLYIGFLGYCSGLIDNLIRRRPIATAGLHR
               :..:.......:::::::::::::::::: ..::::::::::: ::::::.  :::::
SEQ ID NO:514 MMTGRQGRATFQFLPDEARSLPPPKLTDPRLAFVGFLGYCSGLIDNAIRRRPVLLAGLHR
                       10        20        30        40        50        60

              60        70
SEQ ID NO:226 QLLYITAFFLLDIIL
              :::::::.: ...  :
SEQ ID NO:514 QLLYITSFVFVGYYLLKRQDYMYAVRDHDMFSYIKSHPEDFPEKDKKTYGEVFEEFHPVR
                       70        80        90       100       110       120
```

FIGURE 15

<110> Dumas Milne Edwards, Jean-Baptiste
Duclert, Aymeric
Bougueleret, Lydie

<120> Extended cDNAS for Secreted Proteins

<130> GENSET.019A

<160> 519

<170> Patent.pm

<210> 1
<211> 47
<212> RNA
<213> Artificial Sequence

<220>
<221> In vitro transcription product
<221> modified_base
<222> (1)...(1)
<223> m7g

<400> 1
ngcauccuac ucccauccaa uuccacccua acuccuccca ucuccac 47

<210> 2
<211> 46
<212> RNA
<213> Artificial Sequence

<220>
<223> In vitro transcription product

<400> 2
gcauccuacu cccauccaau uccacccuaa cuccucccau cuccac 46

<210> 3
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> In vitro transcription product

<400> 3
atcaagaatt cgcacgagac catta 25

<210> 4
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 4
taatggtctc gtgcgaattc ttgat 25

<210> 5
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
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<400> 5
ccgacaagac caacgtcaag gccgc 25

<210> 6
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 6
tcaccagcag gcagtggctt aggag 25

<210> 7
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
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<400> 7
agtgattcct gctactttgg atggc 25

<210> 8
<211> 25
<212> DNA
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<220>
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<400> 8
gcttggtctt gttctggagt ttaga 25

<210> 9

<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 9
tccagaatgg gagacaagcc aattt 25

<210> 10
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 10
agggaggagg aaacagcgtg agtcc 25

<210> 11
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
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<400> 11
atgggaaagg aaaagactca tatca 25

<210> 12
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 12
agcagcaaca atcaggacag cacag 25

<210> 13
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 13
atcaagaatt cgcacgagac catta 25

<210> 14
<211> 67
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 14
atcgttgaga ctcgtaccag cagagtcacg agagagacta cacggtactg gttttttttt 60
tttttvn 67

<210> 15
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 15
ccagcagagt cacgagagag actacacgg 29

<210> 16
<211> 25
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide

<400> 16
cacgagagag actacacggt actgg 25

<210> 17
<211> 526
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> complement(261..376)
<223> blastn

<221> misc_feature
<222> complement(380..486)
<223> blastn

<221> misc_feature
<222> complement(110..145)
<223> blastn

<221> misc_feature
<222> complement(196..229)
<223> blastn

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<221> sig_peptide
<222> 90..140
<223> Von Heijne matrix

<400> 17
aatatrarac agctacaata ttccagggcc artcacttgc catttctcat aacagcgtca      60
gagagaaaga actgactgar acgtttgag atg aag aaa gtt ctc ctc ctg atc       113
                                Met Lys Lys Val Leu Leu Leu Ile
                                        -15                 -10
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag       161
Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln
                -5                  1                   5
gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr       209
Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly
        10                  15                  20
wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att       257
Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile
    25                  30                  35
cca ttt cca aga ttt cca tgg ttt aga cgt aan ttt cct att cca ata       305
Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Xaa Phe Pro Ile Pro Ile
40                  45                  50                  55
cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa        354
Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys
                60                  65
ggaaaagtca crataaacct ggtcacctga aattgaaatt gagccacttc cttgaaraat     414
caaaattcct gttaataaaa raaaaacaaa tgtaattgaa atagcacaca gcattctcta     474
gtcaatatct ttagtgatct tctttaataa acatgaaagc aaaaaaaaaa aa             526


<210> 18
<211> 17
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..17
<223> Von Heijne matrix
      score 8.2
      seq LLLITAILAVAVG/FP

<400> 18
Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val
1               5                   10                  15
Gly


<210> 19
<211> 822
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 260..464
<223> blastn

<221> misc_feature
<222> 118..184
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<223> blastn

<221> misc_feature
<222> 56..113
<223> blastn

<221> misc_feature
<222> 454..485
<223> blastn

<221> misc_feature
<222> 118..545
<223> blastn

<221> misc_feature
<222> 65..369
<223> blastn

<221> misc_feature
<222> 61..399
<223> blastn

<221> misc_feature
<222> 408..458
<223> blastn

<221> misc_feature
<222> 60..399
<223> blastn

<221> misc_feature
<222> 393..432
<223> blastn

<221> sig_peptide
<222> 346..408
<223> Von Heijne matrix

<400> 19
actcctttta gcataggggc ttcggcgcca gcggccagcg ctagtcggtc tggtaagtgc 60
ctgatgccga gttccgtctc tcgcgtcttt tcctggtccc aggcaaagcg gasgnagatc 120
ctcaaacggc ctagtgcttc gcgcttccgg agaaaatcag cggtctaatt aattcctctg 180
gtttgttgaa gcagttacca agaatcttca acccttttccc acaaaagcta attgagtaca 240
cgttcctgtt gagtacacgt tcctgttgat ttacaaaagg tgcaggtatg agcaggtctg 300
aagactaaca ttttgtgaag ttgtaaaaca gaaaacctgt tagaa atg tgg tgg ttt 357
Met Trp Trp Phe
-20

cag caa ggc ctc agt ttc ctt cct tca gcc ctt gta att tgg aca tct 405
Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val Ile Trp Thr Ser
-15 -10 -5

gct gct ttc ata ttt tca tac att act gca gta aca ctc cac cat ata 453
Ala Ala Phe Ile Phe Ser Tyr Ile Thr Ala Val Thr Leu His His Ile
1 5 10 15

gac ccg gct tta cct tat atc agt gac act ggt aca gta gct cca raa 501
Asp Pro Ala Leu Pro Tyr Ile Ser Asp Thr Gly Thr Val Ala Pro Xaa
20 25 30

aaa tgc tta ttt ggg gca atg cta aat att gcg gca gtt tta tgt caa 549
Lys Cys Leu Phe Gly Ala Met Leu Asn Ile Ala Ala Val Leu Cys Gln
35 40 45

aaa tagaaatcag gaarataatt caacttaaag aakttcattt catgaccaaa 602
Lys

ctcttcaraa acatgtcttt acaagcatat ctcttgtatt gctttctaca ctgttgaatt 662

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gtctggcaat atttctgcag tggaaaattt gatttarmta gttcttgact gataaatatg    722
gtaaggtggg cttttccccc tgtgtaattg gctactatgt cttactgagc caagttgtaw    782
tttgaaataa aatgatatga gagtgacaca aaaaaaaaa                           822


<210> 20
<211> 21
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..21
<223> Von Heijne matrix
      score 5.5
      seq SFLPSALVIWTSA/AF

<400> 20
Met Trp Trp Phe Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val
1               5                   10                  15
Ile Trp Thr Ser Ala
            20



<210> 21
<211> 405
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> complement(103..398)
<223> blastn

<221> sig_peptide
<222> 185..295
<223> Von Heijne matrix

<400> 21
atcaccttct tctccatcct tstctgggcc agtccccarc ccagtccctc tcctgacctg     60
cccagcccaa gtcagccttc agcacgcgct tttctgcaca cagatattcc aggcctacct    120
ggcattccag gacctccgma atgatgctcc agtcccttac aagcgcttcc tggatgaggg    180
tggc atg gtg ctg acc acc ctc ccc ttg ccc tct gcc aac agc cct gtg     229
     Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val
             -35                 -30                 -25
aac atg ccc acc act ggc ccc aac agc ctg agt tat gct agc tct gcc      277
Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala
        -20                 -15                 -10
ctg tcc ccc tgt ctg acc gct cca aak tcc ccc cgg ctt gct atg atg      325
Leu Ser Pro Cys Leu Thr Ala Pro Xaa Ser Pro Arg Leu Ala Met Met
    -5                  1               5                   10
cct gac aac taaatatcct tatccaaatc aataaarwra raatcctccc              374
Pro Asp Asn
tccaraaggg tttctaaaaa caaaaaaaaa a                                   405


<210> 22
<211> 37
<212> PRT
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<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..37
<223> Von Heijne matrix
score 5.9
seq LSYASSALSPCLT/AP

<400> 22
Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
1 5 10 15
Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
20 25 30
Ser Pro Cys Leu Thr
35

<210> 23
<211> 496
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 149..331
<223> blastn

<221> misc_feature
<222> 328..485
<223> blastn

<221> misc_feature
<222> complement(182..496)
<223> blastn

<221> sig_peptide
<222> 196..240
<223> Von Heijne matrix

<400> 23
aaaaaattgg tcccagtttt caccctgccg cagggctggc tggggagggc agcggtttag 60
attagccgtg gcctaggccg tttaacgggg tgacacgagc ntgcagggcc gagtccaagg 120
cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag 180
gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt 231
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe
-15 -10 -5
gcc ara gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt 279
Ala Xaa Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser
1 5 10
gag aag cac aga ctc gag aaa tgt agg gaa ctc gag asc asc cac tcg 327
Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Xaa Xaa His Ser
15 20 25
gcc cca gga tca acc cas cac cga aga aaa aca acc aga aga aat tat 375
Ala Pro Gly Ser Thr Xaa His Arg Arg Lys Thr Thr Arg Arg Asn Tyr
30 35 40 45
tct tca gcc tgaaatgaak ccgggatcaa atggttgctg atcaragccc 424
Ser Ser Ala
atatttaaat tggaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc 484
aaacaaaaaa aa 496

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<210> 24
<211> 15
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..15
<223> Von Heijne matrix
      score 5.5
      seq ILSTVTALTFAXA/LD

<400> 24
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Xaa Ala
1               5                   10                  15



<210> 25
<211> 623
<212> DNA
<213> Homo sapiens

<220>
<221> sig_peptide
<222> 49..96
<223> Von Heijne matrix

<400> 25
aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg      57
                                                     Met Glu Arg
                                                         -15
ctc gtc cta acc ctg tgc acc ctc ccg ctg gct gtg gcg tct gct ggc      105
Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly
            -10                 -5                  1
tgc gcc acg acg cca gct cgc aac ctg agc tgc tac cag tgc ttc aag      153
Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys
    5                   10                  15
gtc agc agc tgg acg gag tgc ccg ccc acc tgg tgc agc ccg ctg gac      201
Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser Pro Leu Asp
20                  25                  30                  35
caa gtc tgc atc tcc aac gag gtg gtc gtc tct ttt aaa tgg agt gta      249
Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Lys Trp Ser Val
                40                  45                  50
cgc gtc ctg ctc agc aaa cgc tgt gct ccc aga tgt ccc aac gac aac      297
Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro Asn Asp Asn
            55                  60                  65
atg aak ttc gaa tgg tcg ccg gcc ccc atg gtg caa ggc gtg atc acc      345
Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly Val Ile Thr
        70                  75                  80
agg cgc tgc tgt tcc tgg gct ctc tgc aac agg gca ctg acc cca cag      393
Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu Thr Pro Gln
    85                  90                  95
gag ggg cgc tgg gcc ctg cra ggg ggg ctc ctg ctc cag gac cct tcg      441
Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Leu Gln Asp Pro Ser
100                 105                 110                 115
agg ggc ara aaa acc tgg gtg cgg cca cag ctg ggg ctc cca ctc tgc      489
Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu Pro Leu Cys
                120                 125                 130
ctt ccc awt tcc aac ccc ctc tgc cca rgg gaa acc cag gaa gga          534
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Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln Glu Gly
135 140 145
taacactgtg ggtgcccccca cctgtgcatt gggaccacra cttcaccctc ttggaracaa 594
taaactctca tgccccccaaa aaaaaaaaa 623

<210> 26
<211> 16
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..16
<223> Von Heijne matrix
score 10.1
seq LVLTLCTLPLAVA/SA

<400> 26
Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala
1 5 10 15

<210> 27
<211> 848
<212> DNA
<213> Homo sapiens

<220>
<221> sig_peptide
<222> 32..73
<223> Von Heijne matrix

<400> 27
aactttgcct tgtgttttcc accctgaaag a atg ttg tgg ctg ctc ttt ttt 52
Met Leu Trp Leu Leu Phe Phe
-10
ctg gtg act gcc att cat gct gaa ctc tgt caa cca ggt gca gaa aat 100
Leu Val Thr Ala Ile His Ala Glu Leu Cys Gln Pro Gly Ala Glu Asn
-5 1 5
gct ttt aaa gtg aga ctt agt atc aga aca gct ctg gga gat aaa gca 148
Ala Phe Lys Val Arg Leu Ser Ile Arg Thr Ala Leu Gly Asp Lys Ala
10 15 20 25
tat gcc tgg gat acc aat gaa gaa tac ctc ttc aaa gcg atg gta gct 196
Tyr Ala Trp Asp Thr Asn Glu Glu Tyr Leu Phe Lys Ala Met Val Ala
30 35 40
ttc tcc atg aga aaa gtt ccc aac aga gaa gca aca gaa att tcc cat 244
Phe Ser Met Arg Lys Val Pro Asn Arg Glu Ala Thr Glu Ile Ser His
45 50 55
gtc cta ctt tgc aat gta acc cag agg gta tca ttc tgg ttt gtg gtt 292
Val Leu Leu Cys Asn Val Thr Gln Arg Val Ser Phe Trp Phe Val Val
60 65 70
aca gac cct tca aaa aat cac acc ctt cct gct gtt gag gtg caa tca 340
Thr Asp Pro Ser Lys Asn His Thr Leu Pro Ala Val Glu Val Gln Ser
75 80 85
gcc ata aga atg aac aag aac cgg atc aac aat gcc ttc ttt cta aat 388
Ala Ile Arg Met Asn Lys Asn Arg Ile Asn Asn Ala Phe Phe Leu Asn
90 95 100 105
gac caa act ctg gaa ttt tta aaa atc cct tcc aca ctt gca cca ccc 436
Asp Gln Thr Leu Glu Phe Leu Lys Ile Pro Ser Thr Leu Ala Pro Pro

110 115 120
atg gac cca tct gtg ccc atc tgg att att ata ttt ggt gtg ata ttt 484
Met Asp Pro Ser Val Pro Ile Trp Ile Ile Ile Phe Gly Val Ile Phe
125 130 135
tgc atc atc ata gtt gca att gca cta ctg att tta tca ggg atc tgg 532
Cys Ile Ile Ile Val Ala Ile Ala Leu Leu Ile Leu Ser Gly Ile Trp
140 145 150
caa cgt ada ara aag aac aaa gaa cca tct gaa gtg gat gac gct gaa 580
Gln Arg Xaa Xaa Lys Asn Lys Glu Pro Ser Glu Val Asp Asp Ala Glu
155 160 165
rat aak tgt gaa aac atg atc aca att gaa aat ggc atc ccc tct gat 628
Xaa Xaa Cys Glu Asn Met Ile Thr Ile Glu Asn Gly Ile Pro Ser Asp
170 175 180 185
ccc ctg gac atg aag gga ggg cat att aat gat gcc ttc atg aca gag 676
Pro Leu Asp Met Lys Gly Gly His Ile Asn Asp Ala Phe Met Thr Glu
190 195 200
gat gag agg ctc acc cct ctc tgaagggctg ttgttctgct tcctcaaraa 727
Asp Glu Arg Leu Thr Pro Leu
205
attaaacatt tgtttctgtg tgactgctga gcatcctgaa ataccaagag cagatcatat 787
wttttgtttc accattcttc ttttgtaata aattttgaat gtgcttgaaa aaaaaaaaaa 847
c 848

<210> 28
<211> 14
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> 1..14
<223> Von Heijne matrix
score 10.7
seq LWLLFFLVTAIHA/EL

<400> 28
Met Leu Trp Leu Leu Phe Phe Leu Val Thr Ala Ile His Ala
1 5 10

<210> 29
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 29
gggaagatgg agatagtatt gcctg 25

<210> 30
<211> 26
<212> DNA
<213> Artificial Sequence

<220>

<223> Olignucleotide

<400> 30
ctgccatgta catgatagag agattc 26

<210> 31
<211> 546
<212> DNA
<213> Homo sapiens

<220>
<221> promoter
<222> 1..517

<221> transcription start site
<222> 518

<221> protein_bind
<222> 17..25
<223> matinspector prediction
name CMYB_01
score 0.983
sequence tgtcagttg

<221> protein_bind
<222> complement(18..27)
<223> matinspector prediction
name MYOD_Q6
score 0.961
sequence cccaactgac

<221> protein_bind
<222> complement(75..85)
<223> matinspector prediction
name S8_01
score 0.960
sequence aatagaattag

<221> protein_bind
<222> 94..104
<223> matinspector prediction
name S8_01
score 0.966
sequence aactaaattag

<221> protein_bind
<222> complement(129..139)
<223> matinspector prediction
name DELTAEF1_01
score 0.960
sequence gcacacctcag

<221> protein_bind
<222> complement(155..165)
<223> matinspector prediction
name GATA_C
score 0.964
sequence agataaatcca

<221> protein_bind

<222> 170..178
<223> matinspector prediction
name CMYB_01
score 0.958
sequence cttcagttg

<221> protein_bind
<222> 176..189
<223> matinspector prediction
name GATA1_02
score 0.959
sequence ttgtagataggaca

<221> protein_bind
<222> 180..190
<223> matinspector prediction
name GATA_C
score 0.953
sequence agataggacat

<221> protein_bind
<222> 284..299
<223> matinspector prediction
name TAL1ALPHAE47_01
score 0.973
sequence cataacagatggtaag

<221> protein_bind
<222> 284..299
<223> matinspector prediction
name TAL1BETAE47_01
score 0.983
sequence cataacagatggtaag

<221> protein_bind
<222> 284..299
<223> matinspector prediction
name TAL1BETAITF2_01
score 0.978
sequence cataacagatggtaag

<221> protein_bind
<222> complement(287..296)
<223> matinspector prediction
name MYOD_Q6
score 0.954
sequence accatctgtt

<221> protein_bind
<222> complement(302..314)
<223> matinspector prediction
name GATA1_04
score 0.953
sequence tcaagataaagta

<221> protein_bind
<222> 393..405
<223> matinspector prediction
name IK1_01
score 0.963
sequence agttgggaattcc

<221> protein_bind
<222> 393..404
<223> matinspector prediction
name IK2_01
score 0.985
sequence agttgggaattc

<221> protein_bind
<222> 396..405
<223> matinspector prediction
name CREL_01
score 0.962
sequence tgggaattcc

<221> protein_bind
<222> 423..436
<223> matinspector prediction
name GATA1_02
score 0.950
sequence tcagtgatatggca

<221> protein_bind
<222> complement(478..489)
<223> matinspector prediction
name SRY_02
score 0.951
sequence taaaacaaaaca

<221> protein_bind
<222> 486..493
<223> matinspector prediction
name E2F_02
score 0.957
sequence tttagcgc

<221> protein_bind
<222> complement(514..521)
<223> matinspector prediction
name MZF1_01
score 0.975
sequence tgagggga

<400> 31
tgagtgcagt gttacatgtc agttgggtta agtttgttaa tgtcattcaa atcttctatg 60
tcttgatttg cctgctaatt ctattatttc tggaactaaa ttagtttgat ggttctatta 120
gttattgact gaggtgtgct aatctcccat tatgtggatt tatctatttc ttcagttgta 180
gataggacat tgatagatac ataagtacca ggacaaaagc agggagatct tttttccaaa 240
atcaggagaa aaaaatgaca tctggaaaac ctatagggaa aggcataaca gatggtaagg 300
atactttatc ttgagtagga gagccttcct gtggcaacgt ggagaaggga agaggtcgta 360
gaattgagga gtcagctcag ttagaagcag ggagttggga attccgttca tgtgatttag 420
catcagtgat atggcaaatg tgggactaag ggtagtgatc agagggttaa aattgtgtgt 480
tttgttttag cgctgctggg gcatcgcctt gggtcccctc aaacagattc ccatgaatct 540
cttcat 546

<210> 32
<211> 23
<212> DNA
<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 32
gtaccaggga ctgtgaccat tgc 23

<210> 33
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 33
ctgtgaccat tgctcccaag agag 24

<210> 34
<211> 861
<212> DNA
<213> Homo sapiens

<220>
<221> promoter
<222> 1..806

<221> transcription start site
<222> 807

<221> protein_bind
<222> complement(60..70)
<223> matinspector prediction
name NFY_Q6
score 0.956
sequence ggaccaatcat

<221> protein_bind
<222> 70..77
<223> matinspector prediction
name MZF1_01
score 0.962
sequence cctgggga

<221> protein_bind
<222> 124..132
<223> matinspector prediction
name CMYB_01
score 0.994
sequence tgaccgttg

<221> protein_bind
<222> complement(126..134)
<223> matinspector prediction
name VMYB_02
score 0.985
sequence tccaacggt

<221> protein_bind
<222> 135..143

```
<223> matinspector prediction
      name STAT_01
      score 0.968
      sequence ttcctggaa

<221> protein_bind
<222> complement(135..143)
<223> matinspector prediction
      name STAT_01
      score 0.951
      sequence ttccaggaa

<221> protein_bind
<222> complement(252..259)
<223> matinspector prediction
      name MZF1_01
      score 0.956
      sequence ttgggga

<221> protein_bind
<222> 357..368
<223> matinspector prediction
      name IK2_01
      score 0.965
      sequence gaatgggatttc

<221> protein_bind
<222> 384..391
<223> matinspector prediction
      name MZF1_01
      score 0.986
      sequence agagggga

<221> protein_bind
<222> complement(410..421)
<223> matinspector prediction
      name SRY_02
      score 0.955
      sequence gaaaacaaaaca

<221> protein_bind
<222> 592..599
<223> matinspector prediction
      name MZF1_01
      score 0.960
      sequence gaagggga

<221> protein_bind
<222> 618..627
<223> matinspector prediction
      name MYOD_Q6
      score 0.981
      sequence agcatctgcc

<221> protein_bind
<222> 632..642
<223> matinspector prediction
      name DELTAEF1_01
      score 0.958
      sequence tcccaccttcc

<221> protein_bind
```

<222> complement(813..823)
<223> matinspector prediction
name S8_01
score 0.992
sequence gaggcaattat

<221> protein_bind
<222> complement(824..831)
<223> matinspector prediction
name MZF1_01
score 0.986
sequence agaggga

<400> 34
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tactataggg cacgcgtggt cgacggccgg gctgttctgg agcagagggc atgtcagtaa      60
tgattggtcc ctggggaagg tctggctggc tccagcacag tgaggcattt aggtatctct     120
cggtgaccgt tggattcctg gaagcagtag ctgttctgtt tggatctggt agggacaggg     180
ctcagagggc taggcacgag ggaaggtcag aggagaaggs aggsarggcc cagtgagarg     240
ggagcatgcc ttccccccaac cctggcttsc ycttggymam agggcgktty tgggmacttr    300
aaytcagggc ccaascagaa scacaggccc aktcntggct smaagcacaa tagcctgaat     360
gggatttcag gttagncagg gtgagagggg aggctctctg gcttagtttt gttttgtttt     420
ccaaatcaag gtaacttgct cccttctgct acgggccttg gtcttggctt gtcctcaccc     480
agtcggaact ccctaccact ttcaggagag tggttttagg cccgtggggc tgttctgttc     540
caagcagtgt gagaacatgg ctggtagagg ctctagctgt gtgcggggcc tgaaggggag     600
tgggttctcg cccaaagagc atctgcccat ttcccacctt cccttctccc accagaagct     660
tgcctgagct gtttggacaa aaatccaaac cccacttggc tactctggcc tggcttcagc     720
ttggaaccca atacctaggc ttacaggcca tcctgagcca ggggcctctg gaaattctct     780
tcctgatggt cctttaggtt tgggcacaaa atataattgc ctctcccctc tcccattttc     840
tctcttggga gcaatggtca c                                               861
```

<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 35
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ctgggatgga aggcacggta                                                  20
```

<210> 36
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 36
```
gagaccacac agctagacaa                                                  20
```

<210> 37
<211> 555
<212> DNA
<213> Homo sapiens

<220>
<221> promoter
<222> 1..500

<221> transcription start site
<222> 501

<221> protein_bind
<222> 191..206
<223> matinspector prediction
name ARNT_01
score 0.964
sequence ggactcacgtgctgct

<221> protein_bind
<222> 193..204
<223> matinspector prediction
name NMYC_01
score 0.965
sequence actcacgtgctg

<221> protein_bind
<222> 193..204
<223> matinspector prediction
name USF_01
score 0.985
sequence actcacgtgctg

<221> protein_bind
<222> complement(193..204)
<223> matinspector prediction
name USF_01
score 0.985
sequence cagcacgtgagt

<221> protein_bind
<222> complement(193..204)
<223> matinspector prediction
name NMYC_01
score 0.956
sequence cagcacgtgagt

<221> protein_bind
<222> complement(193..204)
<223> matinspector prediction
name MYCMAX_02
score 0.972
sequence cagcacgtgagt

<221> protein_bind
<222> 195..202
<223> matinspector prediction
name USF_C
score 0.997
sequence tcacgtgc

<221> protein_bind
<222> complement(195..202)
<223> matinspector prediction
name USF_C
score 0.991

sequence gcacgtga

<221> protein_bind
<222> complement(210..217)
<223> matinspector prediction
name MZF1_01
score 0.968
sequence catgggga

<221> protein_bind
<222> 397..410
<223> matinspector prediction
name ELK1_02
score 0.963
sequence ctctccggaagcct

<221> protein_bind
<222> 400..409
<223> matinspector prediction
name CETS1P54_01
score 0.974
sequence tccggaagcc

<221> protein_bind
<222> complement(460..470)
<223> matinspector prediction
name AP1_Q4
score 0.963
sequence agtgactgaac

<221> protein_bind
<222> complement(460..470)
<223> matinspector prediction
name AP1FJ_Q2
score 0.961
sequence agtgactgaac

<221> protein_bind
<222> 547..555
<223> matinspector prediction
name PADS_C
score 1.000
sequence tgtggtctc

<400> 37
ctatagggca cgcktggtcg acggcccggg ctggtctggt ctgtkgtgga gtcgggttga 60
aggacagcat ttgtkacatc tggtctactg caccttccct ctgccgtgca cttggccttt 120
kawaagctca gcaccggtgc ccatcacagg gccggcagca cacacatccc attactcaga 180
aggaactgac ggactcacgt gctgctccgt ccccatgagc tcagtggacc tgtctatgta 240
gagcagtcag acagtgcctg ggatagagtg agagttcagc cagtaaatcc aagtgattgt 300
cattcctgtc tgcattagta actcccaacc tagatgtgaa aacttagttc tttctcatag 360
gttgctctgc ccatggtccc actgcagacc caggcactct ccggaagcct ggaaatcacc 420
cgtgtcttct gcctgctccc gctcacatcc cacacttgtg ttcagtcact gagttacaga 480
ttttgcctcc tcaatttctc ttgtcttagt cccatcctct gttcccctgg ccagtttgtc 540
tagctgtgtg gtctc 555

<210> 38
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 38
ggccatacac ttgagtgac 19

<210> 39
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 39
atatagacaa acgcacacc 19

<210> 40
<211> 568
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 7..471

<221> sig_peptide
<222> 7..99
<223> Von Heijne matrix
score 6.9
seq LLLVPSALSLLLA/LL

<221> polyA_signal
<222> 537..542

<221> polyA_site
<222> 554..568

<400> 40
gggacc atg ttc acc agc acc ggc tcc agt ggg ctc tac aag gcg cct 48
Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro
-30 -25 -20
ctg tcg aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc 96
Leu Ser Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu
-15 -10 -5
gcc ctc ctc ctg cct cac tgc cag aag ccc ttt gtg tat gac ctt cac 144
Ala Leu Leu Leu Pro His Cys Gln Lys Pro Phe Val Tyr Asp Leu His
1 5 10 15
gca gtc aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata 192
Ala Val Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile
20 25 30
att tgc ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat 240
Ile Cys Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr
35 40 45
aat ttt agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc 288
Asn Phe Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser
50 55 60

```
ttt ttg ctg ggt acc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc      336
Phe Leu Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu
    65                  70                  75
att gaa gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg      384
Ile Glu Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu
80                  85                  90                  95
cct tct gga tta atc ttt tgt tgt gct ttt tgc tct gag act aaa ctc      432
Pro Ser Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu
                100                 105                 110
ttc tta tca aga caa gct atg gca gag aac ttt tcc atc taataaattt       481
Phe Leu Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile
            115                 120
aagagtagat tcatctgtat ggttgagagt aggctctgac tatgtatatg tgtataataa    541
acctacatat ccaaaaaaaa aaaaaaa                                        568
```

```
<210> 41
<211> 569
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 168..332

<221> polyA_signal
<222> 557..562

<400> 41
aggggggcgtg gggccatggt ggtcttgcgg gcggggaaga agacctttct cccccctctc    60
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg    120
gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac      176
                                                    Met Ala Asp
                                                    1
ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat      224
Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr
    5                   10                  15
aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga      272
Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly
20                  25                  30                  35
aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag      320
Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys
                40                  45                  50
aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac          372
Lys Arg Ser Asn
            55
aggaagcaga tggagctcct ttcacagggg ctctgagaaa aactggagcc gatctcaaga    432
agccccacat cttcctaagg ggccccatgg cctgtttggg ggcagggtag gtcctggggc    492
actgtgggcc gcctgcctgc tgatgtgggc tctaggccag cttgttgtca cgtacgtggt    552
gtgaaataaa gcccaag                                                   569
```

```
<210> 42
<211> 895
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 51..251
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<221> sig_peptide
<222> 51..110
<223> Von Heijne matrix
score 5.3
seq ALIFGGFISLIGA/AF

<221> polyA_signal
<222> 849..854

<221> polyA_site
<222> 882..895

<400> 42
```
ccgagagtgc cgggcggtcg gcgggtcagg gcagcccggg gcctgacgcc atg tcc        56
                                                       Met Ser
                                                       -20
cgg aac ctg cgc acc gcg ctc att ttc ggc ggc ttc atc tcc ctg atc      104
Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser Leu Ile
            -15                 -10                 -5
ggc gcc gcc ttc tat ccc atc tac ttc cgg ccc cta atg aga ttg gag      152
Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg Leu Glu
        1               5                   10
gag tac aag aag gaa caa gct ata aat cgg gct gga att gtt caa gag      200
Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val Gln Glu
15                  20                  25                  30
gat gtg cag cca cca ggg tta aaa gtg tgg tct gat cca ttt ggc agg      248
Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe Gly Arg
                35                  40                  45
aaa tgagagggct gtcatcagct ctgattaaga aaggagattt cttcatgctt           301
Lys
tcgattctgc atggggtaca gccagtcacc tcaccagaga atgacggctg gagaagaaaa    361
ctctgtaata ccataaataa gagtgcttgt aataaaagac tgtgcacaag gattaatatt    421
tcccttctta agtatcaaaa gaactctgga acaaattata ccattaggaa ggttttcatg    481
attcagttga ttttccaaaa atgaagctat ctcacccagc tgggtttgga ggagcaatct    541
gcttattatt ctgtcgttac cacttactca agcgagctgt gatatgaata caagcaacca    601
gtgggctcgg gaaggtccgg gtctcttctg ccatcttcca gataagagat ttcagtaaaa    661
aactgccatg ctgagctgcc ttatagagct cttcgaaaat gttcgagttg ataaagctct    721
ttgaggacaa ggtacttcgt gcacctcatg ctgaagattg caccatgttg gaagataaat    781
atgaagcaag tcaaactaga tgcatacact tgtgtagaaa tcaataatca attaatagaa    841
gtgaaaaaat agacattaag atgatttatt tccactttgc aaaaaaaaaa aaaa          895
```

<210> 43
<211> 691
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 20..613

<221> sig_peptide
<222> 20..82
<223> Von Heijne matrix
score 10
seq LWALAMVTRPASA/AP

<400> 43
```
ataccttaga ccctcagtc atg cca gtg cct gct ctg tgc ctg ctc tgg gcc      52
                     Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala
```

-20 -15
ctg gca atg gtg acc cgg cct gcc tca gcg gcc ccc atg ggc ggc cca 100
Leu Ala Met Val Thr Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro
-10 -5 1 5
gaa ctg gca cag cat gag gag ctg acc ctg ctc ttc cat ggg acc ctg 148
Glu Leu Ala Gln His Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu
10 15 20
cag ctg ggc cag gcc ctc aac ggt gtg tac agg acc acg gag gga tgg 196
Gln Leu Gly Gln Ala Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Trp
25 30 35
ctg aca aag gcc agg aac agc ctg ggt ctc tat ggc cgc aca ata gaa 244
Leu Thr Lys Ala Arg Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu
40 45 50
ctc ctg ggg cag gag gtc agc cgg ggc cgg gat gca gcc cag gaa ctt 292
Leu Leu Gly Gln Glu Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu
55 60 65 70
cgg gca agc ctg ttg gag act cag atg gag gag gat att ctg cag ctg 340
Arg Ala Ser Leu Leu Glu Thr Gln Met Glu Glu Asp Ile Leu Gln Leu
75 80 85
cag gca gag gcc aca gct gag gtg ctg ggg gag gtg gcc cag gca cag 388
Gln Ala Glu Ala Thr Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln
90 95 100
aag gtg cta cgg gac agc gtg cag cgg cta gaa gtc cag ctg agg agc 436
Lys Val Leu Arg Asp Ser Val Gln Arg Leu Glu Val Gln Leu Arg Ser
105 110 115
gcc tgg ctg ggc cct gcc tac cga gaa ttt gag gtc tta aag gct cac 484
Ala Trp Leu Gly Pro Ala Tyr Arg Glu Phe Glu Val Leu Lys Ala His
120 125 130
gct gac aag cag agc cac atc cta tgg gcc ctc aca ggc cac gtg cag 532
Ala Asp Lys Gln Ser His Ile Leu Trp Ala Leu Thr Gly His Val Gln
135 140 145 150
cgg cag agg cgg gag atg gtg gca cag cag cat cgg ctg cga cag atc 580
Arg Gln Arg Arg Glu Met Val Ala Gln Gln His Arg Leu Arg Gln Ile
155 160 165
cag gag aga ctc cac aca gcg gcg ctc cca gcc tgaatctgcc tggatggaac 633
Gln Glu Arg Leu His Thr Ala Ala Leu Pro Ala
170 175
tgaggaccaa tcatgctgca aggaacactt ccacgccccg tgaggcccct gtgcaggg 691

<210> 44
<211> 458
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 12..416

<221> sig_peptide
<222> 12..86
<223> Von Heijne matrix
score 4
seq LVVMVPLVGLIHL/GW

<221> polyA_signal
<222> 425..430

<221> polyA_site
<222> 445..458

<400> 44

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gctgaagtac t atg agc ctt cgg aac ttg tgg aga gac tac aaa gtt ttg        50
             Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu
             -25                 -20                 -15
gtt gtt atg gtc cct tta gtt ggg ctc ata cat ttg ggg tgg tac aga         98
Val Val Met Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg
        -10                 -5                  1
atc aaa agc agc cct gtt ttc caa ata cct aaa aac gac gac att cct        146
Ile Lys Ser Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro
5                   10                  15                  20
gag caa gat agt ctg gga ctt tca aat ctt cag aag agc caa atc cag        194
Glu Gln Asp Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln
                25                  30                  35
ggg aag nta gca ggc ttg caa tct tca ggt aaa gaa gca gct ttg aat        242
Gly Lys Xaa Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn
            40                  45                  50
ctg agc ttc ata tcg aaa gaa gag atg aaa aat acc agt tgg att aga        290
Leu Ser Phe Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Ile Arg
        55                  60                  65
aag aac tgg ctt ctt gta gct ggg ata tct ttc ata ggt gac cat ctt        338
Lys Asn Trp Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu
    70                  75                  80
gga aca tac ttt ttg cag agg tct gca aag cag tct gta aaa ttt cag        386
Gly Thr Tyr Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln
85                  90                  95                  100
tct caa agc aaa caa aag agt att gaa gag tgaagtaaaa taaatatttg          436
Ser Gln Ser Lys Gln Lys Ser Ile Glu Glu
                105                 110
gaattactaa aaaaaaaaa aa                                                458
```

<210> 45
<211> 2036
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 276..1040

<221> sig_peptide
<222> 276..485
<223> Von Heijne matrix
score 3.9
seq SVIGVMLAPFTAG/LS

<221> polyA_site
<222> 2024..2036

<400> 45

```
gatcctgggt gcagctcatc acaagcgtcg gggtgcagca aaaccatcca ggctggacag     60
tggctggaca gttccaagaa aagaaacgct tcaccgaaga agtcattgaa tacttccaga    120
agaaagttag cccagtgcat ctgaaaatcc tgctgactag cgatgaagcc tggaagagat    180
tcgtgcgtgt ggctggattg cccagggaag aagcagatgc tctctatgaa gctctgaaga    240
atcttacacc atatgtggct attgaggaca aagac atg cag caa aaa gaa cag       293
                                       Met Gln Gln Lys Glu Gln
                                       -70                 -65
cag ttt agg gag tgg ttt ttg aaa gag ttt cct caa atc aga tgg aag      341
Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe Pro Gln Ile Arg Trp Lys
            -60                 -55                 -50
att cag gag tcc ata gaa agg ctt cgt gtc att gca aat gag att gaa      389
```

```
Ile Gln Glu Ser Ile Glu Arg Leu Arg Val Ile Ala Asn Glu Ile Glu
            -45                 -40                 -35
aag gtc cac aga ggc tgc gtc atc gcc aat gtg gtg tct ggc tcc act       437
Lys Val His Arg Gly Cys Val Ile Ala Asn Val Val Ser Gly Ser Thr
        -30                 -25                 -20
ggc atc ctg tct gtc att ggc gtt atg ttg gca cca ttt aca gca ggg       485
Gly Ile Leu Ser Val Ile Gly Val Met Leu Ala Pro Phe Thr Ala Gly
    -15                 -10                 -5
ctg agc ctg agc att act gca gct ggg gta ggg ctg gga ata gca tct       533
Leu Ser Leu Ser Ile Thr Ala Ala Gly Val Gly Leu Gly Ile Ala Ser
1               5                   10                  15
gcc acg gct ggg atc gcc tcc agc atc gtg gag aac aca tac aca agg       581
Ala Thr Ala Gly Ile Ala Ser Ser Ile Val Glu Asn Thr Tyr Thr Arg
            20                  25                  30
tca gca gaa ctc aca gcc agc agg ctg act gca acc agc act gac caa       629
Ser Ala Glu Leu Thr Ala Ser Arg Leu Thr Ala Thr Ser Thr Asp Gln
        35                  40                  45
ttg gag gca tta agg gac att ctg cat gac atc aca ccc aat gtg ctt       677
Leu Glu Ala Leu Arg Asp Ile Leu His Asp Ile Thr Pro Asn Val Leu
    50                  55                  60
tcc ttt gca ctt gat ttt gac gaa gcc aca aaa atg att gcg aat gat       725
Ser Phe Ala Leu Asp Phe Asp Glu Ala Thr Lys Met Ile Ala Asn Asp
65                  70                  75                  80
gtc cat aca ctc agg aga tct aaa gcc act gtt gga cgc cct ttg att       773
Val His Thr Leu Arg Arg Ser Lys Ala Thr Val Gly Arg Pro Leu Ile
                85                  90                  95
gct tgg cga tat gta cct ata aat gtt gtt gag aca ctg aga aca cgt       821
Ala Trp Arg Tyr Val Pro Ile Asn Val Val Glu Thr Leu Arg Thr Arg
            100                 105                 110
ggg gcc ccc acc cgg ata gtg aga aaa gta gcc cgg aac ctg ggc aag       869
Gly Ala Pro Thr Arg Ile Val Arg Lys Val Ala Arg Asn Leu Gly Lys
        115                 120                 125
gcc act tca ggt gtc ctc gtt gtg ctg gat gta gtc aac ctt gtg caa       917
Ala Thr Ser Gly Val Leu Val Val Leu Asp Val Val Asn Leu Val Gln
    130                 135                 140
gac tca ctg gac ttg cac aag ggg gaa aaa tcc gag tct gct gag ttg       965
Asp Ser Leu Asp Leu His Lys Gly Glu Lys Ser Glu Ser Ala Glu Leu
145                 150                 155                 160
ctg agg cag tgg gct cag gag ctg gag gag aat ctc aat gag ctc acc      1013
Leu Arg Gln Trp Ala Gln Glu Leu Glu Glu Asn Leu Asn Glu Leu Thr
                165                 170                 175
cat atc cat cag agt cta aaa gca ggc taggcccaat tgttgcggga            1060
His Ile His Gln Ser Leu Lys Ala Gly
            180                 185
agtcagggac cccaaacgga gggactggct gaagccatgg cagaagaacg tggattgtga    1120
agatttcatg gacatttatt agttccccaa attaatactt ttataatttc ctatgcctgt    1180
ctttaccgca atctctaaac acaaattgtg aagatttcat ggacacttat cacttcccca    1240
atcaataccc ttgtgatttc ttatgcctgt ctttacttta atctcctaat cctgtcagct    1300
gaggagggtg tatgtcacct caggaccatg tgataattgc gttaactgca caaattgtag    1360
agcatgtgtg tttgaacaat atgaaatctg ggcaccttga aaaaagaaca ggataacagc    1420
aatcgttcag gggataagag agataacctt aaactctgac caacagtgag ccgggtggag    1480
cagagtcata tttcttttct ttcaaaagca aatgggagaa atatcgctga attctttttc    1540
tcagcaagga acatccctga gaaagagaat gcacccctga gggtgggtct ataaatggcc    1600
tccttgggtg tggccatctt ctatggtcga gactgtaggg atgaaataaa ccccagtctc    1660
ccatagtgct cccaggctta ttaggaagag gaaattcccg cctaataaat tttggtcaga    1720
ccggttgctc tcaaaaccct gtctcctgat aagatgttat caatgacaat ggtgcctgaa    1780
acctcattag caattttaat ttctccccgg tcctgtggtc ctgtgatctc accctgcctc    1840
cacttgcctt gtgatattct attaccttgt gaagtaggtg atctttgtga cccacaccct    1900
attcatacac tccctcccct tttggaagtc cctaataaaa acttgctggt tttgcagctt    1960
gtgaggcatc acggaaccta ctgatgtgtg atgtctcccc tggacaccta gctttaaaat    2020
ttcaaaaaaa aaaaaa                                                    2036
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<210> 46
<211> 1276
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 443..619

<221> sig_peptide
<222> 443..589
<223> Von Heijne matrix
      score 7
      seq LICVVCLYIVCRC/GS

<221> polyA_site
<222> 1267..1276

<400> 46
gaggcactca cggcatttca ttgctacttt aattttcatt attatgggat tgattgctgt      60
cacagctact gctgcagtag ctggagttgc tttgcattcc acagtacaaa cagcagacta     120
tgtaaataat tggtagaaaa attctactct gctgtggaat taccaagata atatagacca     180
gaaactagct gatcaaatta atgatctcca acaaactgta atgtggctag ggatcatat      240
agttagttta gaatatagaa tgcggttaca atgtgattga aatacctctg atttttgcat     300
tactcctcat ctgtgtaatg aaacagagca tgagtgggaa aaagttaaga gatatttaaa     360
aggtcatact agaaatttat ctttggatat tgcaaagcta aaggaacaag tatttcaagc     420
ccctcagata catctgacac ta atg cca gga act gaa gtg ctt gaa gga gct      472
                         Met Pro Gly Thr Glu Val Leu Glu Gly Ala
                                             -45                 -40

aca gac gga tta gca gct att aac ctg cta aaa tgg atc aag aca ctt       520
Thr Asp Gly Leu Ala Ala Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu
                -35                 -30                 -25

gga ggc tct gtg att tca atg att gtg ctt tta atc tgt gtt gtt tgt       568
Gly Gly Ser Val Ile Ser Met Ile Val Leu Leu Ile Cys Val Val Cys
            -20                 -15                 -10

ctt tat ata gtc tgt aga tgc gga agc cac ctc tgg aga gaa agc cac       616
Leu Tyr Ile Val Cys Arg Cys Gly Ser His Leu Trp Arg Glu Ser His
        -5                  1               5

cac tgagagcaag caatgatagc tgtggcggtt ttgcaaaaag aaaagggaga            669
His
10
caagcgccca gctatagtta ccaataaagc atggtactgg tattaaaata ggcatgtgtt     729
ctgttccaat ggaacagaat agagaaccca gaaacaaagc caaatattta cagccaactg     789
atctctgaca aagcaaacaa aaacataaag tggggaaagg acaccctatt ccacaaatag     849
tgcagggata attggcaagc cacatgtaga aaaatgaagc tggatcctcg tctctcactt     909
tatacaaaaa tcaactcaaa atgggtcaaa gtcttaactc taagacctga aaccataaca     969
attctagaaa ataacattgg aaaaactctt ctagacattg gtttaggcaa aaagttcatg    1029
accaagaacc caaaagcaaa tgcaataaaa aggaagataa atagatggga cctaattaag    1089
ctgaaaagct tctgcatagc aaaaggaata atcagcagag caaacagaca acccacaggg    1149
tgggagaaaa tatttgcaag ctatgtatct gacaatggac taatatccag aatctacaag    1209
gaattcaaac aattagcaag aaaaaacact tgtattgtgt ttgctctgta aatcagcaaa    1269
aaaaaaa                                                              1276


<210> 47
<211> 747
<212> DNA
<213> Homo sapiens
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<220>
<221> CDS
<222> 206..745

<400> 47
accagaagca ggtgatttcc gagctcagca atgctcagct cataatgatg tcaagcacca 60
tggccagttt tatgaatggc ttcctgtgtc taatgaccct gacaacccat gttcactcaa 120
gtgccaagcc aaaggaacaa ccctggttgt tgaactagca cctaaggtct tagatggtac 180
gcgttgctat acagaatctt tggat atg tgc atc agt ggt tta tgc caa att 232
Met Cys Ile Ser Gly Leu Cys Gln Ile
1 5
gtt ggc tgc gat cac cag ctg gga agc acc gtc aag gaa gat aac tgt 280
Val Gly Cys Asp His Gln Leu Gly Ser Thr Val Lys Glu Asp Asn Cys
10 15 20 25
ggg gtc tgc aac gga gat ggg tcc acc tgc cgg ctg gtc cga ggg cag 328
Gly Val Cys Asn Gly Asp Gly Ser Thr Cys Arg Leu Val Arg Gly Gln
30 35 40
tat aaa tcc cag ctc tcc gca acc aaa tcg gat gat act gtg gtt gca 376
Tyr Lys Ser Gln Leu Ser Ala Thr Lys Ser Asp Asp Thr Val Val Ala
45 50 55
att ccc tat gga agt aga cat att cgc ctt gtc tta aaa ggt cct gat 424
Ile Pro Tyr Gly Ser Arg His Ile Arg Leu Val Leu Lys Gly Pro Asp
60 65 70
cac tta tat ctg gaa acc aaa acc ctc cag ggg act aaa ggt gaa aac 472
His Leu Tyr Leu Glu Thr Lys Thr Leu Gln Gly Thr Lys Gly Glu Asn
75 80 85
agt ctc agc tcc aca gga act ttc ctt gtg gac aat tct agt gtg gac 520
Ser Leu Ser Ser Thr Gly Thr Phe Leu Val Asp Asn Ser Ser Val Asp
90 95 100 105
ttc cag aaa ttt cca gac aaa gag ata ctg aga atg gct gga cca ctc 568
Phe Gln Lys Phe Pro Asp Lys Glu Ile Leu Arg Met Ala Gly Pro Leu
110 115 120
aca gca gat ttc att gtc aag att cgt aac tcg ggc tcc gct gac agt 616
Thr Ala Asp Phe Ile Val Lys Ile Arg Asn Ser Gly Ser Ala Asp Ser
125 130 135
aca gtc cag ttc atc ttc tat caa ccc atc atc cac cga tgg agg gag 664
Thr Val Gln Phe Ile Phe Tyr Gln Pro Ile Ile His Arg Trp Arg Glu
140 145 150
acg gat ttc ttt cct tgc tca gca acc tgt gga gga ggt tat cag ctg 712
Thr Asp Phe Phe Pro Cys Ser Ala Thr Cys Gly Gly Gly Tyr Gln Leu
155 160 165
aca tcg gct gag tgc tac gat ctg agg agc aac cg 747
Thr Ser Ala Glu Cys Tyr Asp Leu Arg Ser Asn
170 175 180

<210> 48
<211> 561
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 36..521

<221> sig_peptide
<222> 36..104
<223> Von Heijne matrix
score 7.4
seq VLLLAALPPVLLP/GA

<221> polyA_signal
<222> 528..533

<221> polyA_site
<222> 548..561

<400> 48
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gacgcctctt tcagcccggg atcgccccag caggg atg ggc gac aag atc tgg        53
                                       Met Gly Asp Lys Ile Trp
                                                   -20
ctg ccc ttc ccc gtg ctc ctt ctg gcc gct ctg cct ccg gtg ctg ctg      101
Leu Pro Phe Pro Val Leu Leu Leu Ala Ala Leu Pro Pro Val Leu Leu
        -15                 -10                 -5
cct ggg gcg gcc ggc ttc aca cct tcc ctc gat agc gac ttc acc ttt      149
Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu Asp Ser Asp Phe Thr Phe
    1               5                   10                  15
acc ctt ccc gcc ggc cag aag gag tgc ttc tac cag ccc atg ccc ctg      197
Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe Tyr Gln Pro Met Pro Leu
                20                  25                  30
aag gcc tcg ctg gag atc gag tac caa gtt tta gat gga gca gga tta      245
Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu
            35                  40                  45
gat att gat ttc cat ctt gcc tct cca gaa ggc aaa acc tta gtt ttt      293
Asp Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe
        50                  55                  60
gaa caa aga aaa tca gat gga gtt cac act gta gag act gaa gtt ggt      341
Glu Gln Arg Lys Ser Asp Gly Val His Thr Val Glu Thr Glu Val Gly
    65                  70                  75
gat tac atg ttc tgc ttt gac aat aca ttc agc acc att tct gag aag      389
Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Lys
80                  85                  90                  95
gtg att ttc ttt gaa tta atc ccg gat aat atg gga gaa cag gca caa      437
Val Ile Phe Phe Glu Leu Ile Pro Asp Asn Met Gly Glu Gln Ala Gln
                100                 105                 110
gaa caa gaa gat tgg aag aaa tat att act ggc aca gat ata ttg gat      485
Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp
            115                 120                 125
atg aaa ctg gaa gac atc ctg gtc agt atg gtc ttc taataaaata           531
Met Lys Leu Glu Asp Ile Leu Val Ser Met Val Phe
        130                 135
aaaattatta acagccaaaa aaaaaaaaaa                                     561
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<210> 49
<211> 632
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 36..395

<221> sig_peptide
<222> 36..104
<223> Von Heijne matrix
score 7.4
seq VLLLAALPPVLLP/GA

<221> polyA_signal
<222> 599..604

<221> polyA_site
<222> 619..632

<400> 49
gacgcctctt tcagcccggg atcgccccag caggg atg ggc gac aag atc tgg 53
Met Gly Asp Lys Ile Trp
-20
ctg ccc ttc ccc gtg ctc ctt ctg gcc gct ctg cct ccg gtg ctg ctg 101
Leu Pro Phe Pro Val Leu Leu Leu Ala Ala Leu Pro Pro Val Leu Leu
-15 -10 -5
cct ggg gcg gcc ggc ttc aca cct tcc ctc gat agc gac ttc acc ttt 149
Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu Asp Ser Asp Phe Thr Phe
1 5 10 15
acc ctt ccc gcc ggc cag aag gag tgc ttc tac cag ccc atg ccc ctg 197
Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe Tyr Gln Pro Met Pro Leu
20 25 30
aag gcc tcg ctg gag atc gag tac caa gtt tta gat gga gca gga tta 245
Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu
35 40 45
gat att gat ttc cat ctt gcc tct cca gaa ggc aaa acc tta gtt ttt 293
Asp Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe
50 55 60
gaa caa aga aaa tca gat gga gtt cac acg tgt ata aga agt aaa aat 341
Glu Gln Arg Lys Ser Asp Gly Val His Thr Cys Ile Arg Ser Lys Asn
65 70 75
ggg cca ggc act gcg gtt cac gcc tat aat ccc agc act ttc cga ggc 389
Gly Pro Gly Thr Ala Val His Ala Tyr Asn Pro Ser Thr Phe Arg Gly
80 85 90 95
caa gtg tagagactga agttggtgat tacatgttct gctttgacaa tacattcagc 445
Gln Val
accatttctg agaaggtgat tttctttgaa ttaatcctgg ataatatggg agaacaggca 505
caaggacaag aagattggaa gaaatatatt actggcacag atatattgga tatgaaactg 565
gaagacatcc tggtcagtat ggtcttctaa taaaataaaa attattaaca gccaaaaaaa 625
aaaaaaa 632

<210> 50
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 21..41

<221> polyA_signal
<222> 328..333

<221> polyA_site
<222> 357..370

<400> 50
ctgggacttc tggcctcaca atg gtt gag atg act ggg gtg tagcagtgcc 51
Met Val Glu Met Thr Gly Val
1 5
aagtcgaggc tgtgaaaggc cttccacctt tactctcgtg ctcgtgccct cccccattgt 111
taggagaagg gcatgctcag gccagcccat tagcccagga ggaggacaag aaacacacgg 171
agcagacaca agccacctca ccaacccagc caaggctgtc ctgaattagc aaccctgaca 231
cgtgtgagca agtccaacgg acaccggaag atccacctag tcaagcccaa ccaagactgg 291
cagagctgcc aagctgacca cttaaggcgc atgaggaata aacactcgtt gctgcatgcc 351
attgcaaaaa aaaaaaaaa 370

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<210> 51
<211> 994
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 35..631

<221> sig_peptide
<222> 35..160
<223> Von Heijne matrix
      score 8.6
      seq ASLFLLLSLTVFS/IV

<221> polyA_signal
<222> 901..906

<221> polyA_site
<222> 979..994

<400> 51
ataattggag ctgcaaagca gatcgtgaca agag atg gac ggt cag aag aaa aat      55
                                      Met Asp Gly Gln Lys Lys Asn
                                                  -40

tgg aag gac aag gtt gtt gac ctc ctg tac tgg aga gac att aag aag       103
Trp Lys Asp Lys Val Val Asp Leu Leu Tyr Trp Arg Asp Ile Lys Lys
-35                 -30                 -25                 -20

act gga gtg gtg ttt ggt gcc agc cta ttc ctg ctg ctt tca ttg aca       151
Thr Gly Val Val Phe Gly Ala Ser Leu Phe Leu Leu Leu Ser Leu Thr
                -15                 -10                 -5

gta ttc agc att gtg agc gta aca gcc tac att gcc ttg gcc ctg ctc       199
Val Phe Ser Ile Val Ser Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu
            1               5                   10

tct gtg acc atc agc ttt agg ata tac aag ggt gtg atc caa gct atc       247
Ser Val Thr Ile Ser Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile
    15                  20                  25

cag aaa tca gat gaa ggc cac cca ttc agg gca tat ctg gaa tct gaa       295
Gln Lys Ser Asp Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu
30                  35                  40                  45

gtt gct ata tct gag gag ttg gtt cag aag tac agt aat tct gct ctt       343
Val Ala Ile Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu
                50                  55                  60

ggt cat gtg aac tgc acg ata aag gaa ctc agg cgc ctc ttc tta gtt       391
Gly His Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val
            65                  70                  75

gat gat tta gtt gat tct ctg aag ttt gca gtg ttg atg tgg gta ttt       439
Asp Asp Leu Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe
        80                  85                  90

acc tat gtt ggt gcc ttg ttt aat ggt ctg aca cta ctg att ttg gct       487
Thr Tyr Val Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu Ala
    95                  100                 105

ctc att tca ctc ttc agt gtt cct gtt att tat gaa cgg cat cag gca       535
Leu Ile Ser Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His Gln Ala
110                 115                 120                 125

cag ata gat cat tat cta gta ctt gca aat aag aat gtt aaa gat gct       583
Gln Ile Asp His Tyr Leu Val Leu Ala Asn Lys Asn Val Lys Asp Ala
                130                 135                 140

atg gct aaa atc caa gca aaa atc cct gga ttg aag cgc aaa gct gaa       631
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Met Ala Lys Ile Gln Ala Lys Ile Pro Gly Leu Lys Arg Lys Ala Glu
        145                 150                 155
tgaaaacgcc caaaataatt agtaggagtt catctttaaa ggggatattc atttgattat    691
acgggggagg gtcagggaag aacgaacctt gacgttgcag tgcagtttca cagatcgttg    751
ttagatcttt atttttagcc atgcactgtt gtgaggaaaa attacctgtc ttgactgcca    811
tgtgttcatc atcttaagta ttgtaagctg ctatgtatgg atttaaaccg taatcatatc    871
tttttcctat ctatctgagg cactggtgga ataaaaaacc tgtatatttt actttgttgc    931
agatagtctt gccgcatctt ggcaagttgc agagatggtg gagctagaaa aaaaaaaaac    991
aaa                                                                  994
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<210> 52
<211> 412
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 271..399

<400> 52

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gccgctagcg cctcgagcga tgcacctcct ttccaactgg gcaaaccccg cttccagcag     60
acgtccttct atggccgctt caggcacttc ttggatatca tcgaccctcg cacactcttt    120
gtcactgaga gacgtctcag agaggctgtg cagctgctgg aggactataa gcatgggacc    180
ctgcgcccgg gggtcaccaa tgaacagctc tggagtgcac agaaaatcaa gcaggctatt    240
ctacatccgg acaccaatga gaagatcttc atg cca ttt aga atg tca ggt tat     294
                                 Met Pro Phe Arg Met Ser Gly Tyr
                                 1               5
att cct ttt ggg acg cca att gta agt gtt acc ttc aaa gga ttt cct      342
Ile Pro Phe Gly Thr Pro Ile Val Ser Val Thr Phe Lys Gly Phe Pro
    10                  15                  20
ttt cta aaa aat tat ttt aaa tgt cta act tta tgt tat tgc tca cgg      390
Phe Leu Lys Asn Tyr Phe Lys Cys Leu Thr Leu Cys Tyr Cys Ser Arg
25                  30                  35                  40
gta ttt gac tgaattgttg att                                           412
Val Phe Asp
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<210> 53
<211> 597
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 103..252

<221> sig_peptide
<222> 103..213
<223> Von Heijne matrix
score 3.9
seq PGPSLRLFSGSQA/SV

<221> polyA_site
<222> 588..597

<400> 53

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gaaaggtcag aggaaggagc tgtgggaagc tcgcagcagg tatcggagct taagccagtg     60
gatttggggg ccctgggctc cctagccggc tgcggtgtga ga atg gag tgg gca       114
                                               Met Glu Trp Ala
```

-35
gga aag cag cgg gac ttt cag gta agg gca gct ccg ggc tgg gat cat 162
Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro Gly Trp Asp His
-30 -25 -20
ttg gcc tcc ttt cct ggc cct tct ctc cgg ctg ttt tct ggg agt cag 210
Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe Ser Gly Ser Gln
-15 -10 -5
gcg agt gtc tgt agt ctc tgc tcg ggg ttt ggg gct cag gaa 252
Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala Gln Glu
1 5 10
tgatgtcatg ctccaacagt tggattctat tagcttaagg aggagggaaa cagccaattt 312
tcttgacttt gcaaatctag ctgatctcac tcttgctgaa tctgaggtgt ttagacttca 372
ctctaaaaag catcatttta cttttattta gcacaaaggc acaggatatt tttacaggaa 432
gaatctttta tatggaaaaa tctgagttaa catcactccc gtggtgtttg tagttcttac 492
agggaaactc cagtgccttt tgagccgctt gttcgtccta gtgaacactg tctgttttgt 552
ctcttggtgc tgctatgtct gacctgtaat gggagaaaaa aagaa 597

<210> 54
<211> 748
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..460

<221> polyA_signal
<222> 713..718

<221> polyA_site
<222> 735..748

<400> 54
c aca gtt cct ctc ctc cta gag cct gcc gac cat gcc cgc ggg cgt gcc 49
Thr Val Pro Leu Leu Leu Glu Pro Ala Asp His Ala Arg Gly Arg Ala
1 5 10 15
cat gtc cac cta cct gaa aat gtt cgc agc cag tct cct ggc cat gtg 97
His Val His Leu Pro Glu Asn Val Arg Ser Gln Ser Pro Gly His Val
20 25 30
cgc agg ggc aga agt ggt gca cag gta cta ccg acc gga cct gat gag 145
Arg Arg Gly Arg Ser Gly Ala Gln Val Leu Pro Thr Gly Pro Asp Glu
35 40 45
aaa cag gtt gag aag agt gaa gtt gat ttc tca aag tca cat agc tta 193
Lys Gln Val Glu Lys Ser Glu Val Asp Phe Ser Lys Ser His Ser Leu
50 55 60
gtg aga cga ttt gag gat ctg aag ccc aag ctt tct gtt tgc aaa act 241
Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Lys Thr
65 70 75 80
gga tca caa gtc ttt cgg tcg gag aac tgg aag gtc tgg gca gag tcg 289
Gly Ser Gln Val Phe Arg Ser Glu Asn Trp Lys Val Trp Ala Glu Ser
85 90 95
agc aga gga gac cat gat gac tgc cta gac ttg tgc tca gtg ctg tgt 337
Ser Arg Gly Asp His Asp Asp Cys Leu Asp Leu Cys Ser Val Leu Cys
100 105 110
tgg gga gaa ctg cta cgg aca ata cct gaa att cca cca aag cgt gga 385
Trp Gly Glu Leu Leu Arg Thr Ile Pro Glu Ile Pro Pro Lys Arg Gly
115 120 125
gaa ctc aaa acg gag ctt ttg gga ctg aaa gaa aga aaa cac aaa cct 433
Glu Leu Lys Thr Glu Leu Leu Gly Leu Lys Glu Arg Lys His Lys Pro
130 135 140

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caa gtt tct caa cag gag gaa ctt aaa taactatgcc aagaattctg          480
Gln Val Ser Gln Gln Glu Glu Leu Lys
145                 150
tgaataatat aagtcttaaa tatgtatttc ttaatttatt gcatcaaact acttgtcctt    540
aagcacttag tctaatgcta actgcaagag gaggtgctca gtggatgttt agccgatacg    600
ttgaaattta attacggttt gattgatatt tcttgaaaac cgccaaagca catatcatca    660
aaccatttca tgaatatggt ttggaagatg tttagtcttg aatataatgc gaaatagaat    720
atttgtaagt ctaccaaaaa aaaaaaaa                                       748
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<210> 55
<211> 703
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 31..231

<221> polyA_signal
<222> 769..774

<221> polyA_site
<222> 690..703

<400> 55
ctctggtggc tctgctacgg cggcgcagaa atg agg cag aag cgg aaa gga gat    54
                                 Met Arg Gln Lys Arg Lys Gly Asp
                                 1               5
ctc agc cct gct aag ctg atg atg ctg act ata gga gat gtt att aaa    102
Leu Ser Pro Ala Lys Leu Met Met Leu Thr Ile Gly Asp Val Ile Lys
    10                  15                  20
caa ctg att gaa gcc cac gag cag ggg aaa gac atc gat cta aat aag    150
Gln Leu Ile Glu Ala His Glu Gln Gly Lys Asp Ile Asp Leu Asn Lys
25                  30                  35                  40
gtg aga acc aag aca gct gcc aaa tat ggc ctt tct gcc cag ccc cgc    198
Val Arg Thr Lys Thr Ala Ala Lys Tyr Gly Leu Ser Ala Gln Pro Arg
                45                  50                  55
ctg gtg gat atc att gct gcc gtc cct cct gag tagctgggat tacaggcacc   251
Leu Val Asp Ile Ile Ala Ala Val Pro Pro Glu
            60                  65
cgccgctgcc aattttttgta tttttagtag ggatgggggt ttcaccatat tggtcaggct   311
ggtctcgaac tcctgacctc aggtgatcaa cccaccttgg cctccctaaa tgccgggatt    371
acaggcatga gccaccgctc cgggcctttg atttttttaag gtggattttg gttgttataa   431
atggagaaag gtaagagttc aagttcaacc cgtgtgtgaa agcaaaacaa tggaaaacag    491
gattggcttc ttcaaaggct cctcttgtag aactgcctct ttgaaatttc gaggtaatct    551
actttggaga ctctgcctgg agagggtcag ttcctaagtt aaaagcatcg cttaaccttg    611
gctcctgtgg cattttacaa aggtttaaag gaattgattc ctctgaaagg gcctgaaaat    671
aaaaagtctt taacatacaa aaaaaaaaaa aa                                  703
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<210> 56
<211> 725
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 305..565
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<221> polyA_signal
<222> 694..699

<221> polyA_site
<222> 713..725

<400> 56
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ctcacggtgg tgaaggtcac agggttgcag cactcccagt agaccaggag ctccgggagg      60
cagggccggc cccacgtcct ctgcgcacca ccctgagttg gatcctctgt gcgccacccc     120
tgagttggat ccagggctag ctgctgttga cctcccact cccacgctgc cctcctgcct      180
gcagccatga cgcccctgct caccctgatc ctggtggtcc tcatgggctt acctctggcc     240
caggccttgg actgccacgt gtgaggacta caaatccctc caggatatca ttgccatcct     300
gggt atg gat gaa ctt tct gag gaa gac aag ttg acc gtg tcc cgt gca      349
     Met Asp Glu Leu Ser Glu Glu Asp Lys Leu Thr Val Ser Arg Ala
     1               5                   10                  15
cgg aaa ata cag cgt ttc ttg tct cag cca ttc cag gtt gct gag gtc       397
Arg Lys Ile Gln Arg Phe Leu Ser Gln Pro Phe Gln Val Ala Glu Val
                20                  25                  30
ttc aca ggt cat atg ggg aag ctg gta ccc ctg aag gag acc atc aaa       445
Phe Thr Gly His Met Gly Lys Leu Val Pro Leu Lys Glu Thr Ile Lys
            35                  40                  45
gga ttc cag cag att ttg gca ggt gaa tat gac cat ctc cca gaa cag       493
Gly Phe Gln Gln Ile Leu Ala Gly Glu Tyr Asp His Leu Pro Glu Gln
        50                  55                  60
gcc ttc tat atg gtg gga ccc att gaa gaa gct gtg gca aaa gct gat       541
Ala Phe Tyr Met Val Gly Pro Ile Glu Glu Ala Val Ala Lys Ala Asp
    65                  70                  75
aag ctg gct gaa gag cat tca tcg tgaggggtct ttgtcctctg tactgtctct      595
Lys Leu Ala Glu Glu His Ser Ser
80                  85
ctccttgccc ctaacccaaa aagcttcatt tttctgtgta ggctgcacaa gagccttgat     655
tgaagatata ttctttctga acagtattta aggtttccaa taaagtgtac acccctcaaa     715
aaaaaaaaaa                                                            725
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<210> 57
<211> 1705
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 124..873

<221> sig_peptide
<222> 124..378
<223> Von Heijne matrix
score 3.6
seq HLSVVTLAAKVKC/IP

<221> polyA_signal
<222> 1673..1678

<221> polyA_site
<222> 1694..1705

<400> 57
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cggaggtgag gagcggcggc cccgcccggt gcgctggagg tcgaagcttc caggtagcgg      60
cccgcagagc ctgacccagg ctctggacat cctgagccca agtcccccac actcagtgca     120
gtg atg agt gcg gaa gtg aag gtg aca ggg cag aac cag gag caa ttt       168
    Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe
```

```
    -85                     -80                     -75
ctg ctc cta gcc aag tcg gcc aag ggg gca gcg ctg gcc aca ctc atc      216
Leu Leu Leu Ala Lys Ser Ala Lys Gly Ala Ala Leu Ala Thr Leu Ile
-70                 -65                     -60                 -55
cat cag gtg ctg gag gcc cct ggt gtc tac gtg ttt gga gaa ctg ctg      264
His Gln Val Leu Glu Ala Pro Gly Val Tyr Val Phe Gly Glu Leu Leu
                -50                     -45                     -40
gac atg ccc aat gtt aga gag ctg naa gcc cgg aat ctt cct cca cta      312
Asp Met Pro Asn Val Arg Glu Leu Xaa Ala Arg Asn Leu Pro Pro Leu
            -35                     -30                     -25
aca gag gct cag aag aat aag ctt cga cac ctc tca gtt gtc acc ctg      360
Thr Glu Ala Gln Lys Asn Lys Leu Arg His Leu Ser Val Val Thr Leu
        -20                     -15                     -10
gct gct aaa gta aag tgt atc cca tat gca gtg ttg ctg gag gct ctt      408
Ala Ala Lys Val Lys Cys Ile Pro Tyr Ala Val Leu Leu Glu Ala Leu
    -5                  1                   5                   10
gcc ctg cgt aat gtg cgg cag ctg gaa gac ctt gtg att gag gct gtg      456
Ala Leu Arg Asn Val Arg Gln Leu Glu Asp Leu Val Ile Glu Ala Val
                15                  20                  25
tat gct gac gtg ctt cgt ggc tcc ctg gac cag cgc aac cag cgg ctc      504
Tyr Ala Asp Val Leu Arg Gly Ser Leu Asp Gln Arg Asn Gln Arg Leu
            30                  35                  40
gag gtt gac tac agc atc ggg cgg gac atc cag cgc cag gac ctc agt      552
Glu Val Asp Tyr Ser Ile Gly Arg Asp Ile Gln Arg Gln Asp Leu Ser
        45                  50                  55
gcc att gcc cga acc ctg cag gaa tgg tgt gtg ggc tgt gag gtc gtg      600
Ala Ile Ala Arg Thr Leu Gln Glu Trp Cys Val Gly Cys Glu Val Val
    60                  65                  70
ctg tca ggc att gag gag cag gtg agc cgt gcc aac caa cac aag gag      648
Leu Ser Gly Ile Glu Glu Gln Val Ser Arg Ala Asn Gln His Lys Glu
75                  80                  85                  90
cag cag ctg ggc ctg aag cag cag att gag agt gag gtt gcc aac ctt      696
Gln Gln Leu Gly Leu Lys Gln Gln Ile Glu Ser Glu Val Ala Asn Leu
                95                  100                 105
aaa aaa acc att aaa gtt acg acg gca gca gca gcc gca gcc aca tct      744
Lys Lys Thr Ile Lys Val Thr Thr Ala Ala Ala Ala Ala Ala Thr Ser
            110                 115                 120
cag gac cct gag caa cac ctg act gag ctg agg gaa cca gct cct ggc      792
Gln Asp Pro Glu Gln His Leu Thr Glu Leu Arg Glu Pro Ala Pro Gly
        125                 130                 135
acc aac cag cgc cag ccc agc aag aaa gcc tca aag ggc aag ggg ctc      840
Thr Asn Gln Arg Gln Pro Ser Lys Lys Ala Ser Lys Gly Lys Gly Leu
    140                 145                 150
cga ggg agc gcc aag att tgg tcc aag tcg aat tgaaagaact gtcgtttcct    893
Arg Gly Ser Ala Lys Ile Trp Ser Lys Ser Asn
155                 160                 165
ccctggggat gtggggtccc agctgcctgc ctgcctctta ggagtcctca gagagccttc    953
tgtgcccctg gccagctgat aatcctaggt tcatgaccct tcacctcccc taaccccaaa    1013
catagatcac accttctcta gggaggagtc aaatgtaggt catgtttttg ttggtacttt    1073
ctgtttttg tgacttcatg tgttccattg ctccccgctg ccatgctctc tcccttgttt    1133
ccttaagagc tcagcatctg tccctgttca ttacatgtca ttgagtaggt gggtagccct    1193
gatgggggtc gctctgtctg gagcataacc cacaggcgtt ttttctgcca ccccatccct    1253
gcatgcctga tccccagttc ctataccta cccctgacct attgagcagc ctctgaagag    1313
ccatagggcc cccaccttta ctcacaccct gagaattctg ggagccagtc tgccatgcca    1373
ggagtcactg gacatgttca tcctagaatc ctgtcacact acagtcattt cttttcctct    1433
ctctggccct tgggtcctgg gaatgctgct gcttcaaccc cagagcctaa gaatggcagc    1493
cgtttcttaa catgttgaga gatgattctt tcttggccct ggccatctcg ggaagcttga    1553
tggcaatcct ggaagggttt aatctccttt tgtgagtttg gtggggaagg gaagggtata    1613
tagattatat taaaaaaaaa aaggtatata tgcatatatc tatatataat atgacgcaga    1673
aataaatcta tgagaaatcc aaaaaaaaaa aa                                  1705
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<210> 58
<211> 1069
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 135..206

<221> polyA_signal
<222> 850..855

<221> polyA_site
<222> 1056..1069

<400> 58
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cccactccgc tctcacgact aagctctcac gattaaggca cgcctgcctc gattgtccag     60
cctctgccag aagaaagctt agcagccagc gcctcagtag agacctaagg gcgctgaatg    120
agtgggaaag ggaa atg ccg acc aat tgc gct gcg gcg ggc tgt gcc act      170
                Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr
                1               5                   10
acc tac aac aag cac att aac atc agc ttc cac agg taacctgggc           216
Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg
        15                  20
agggagtggg ggtgacggaa actggagttc ctattgtggc tatcgcttgt gtggaaggaa    276
caggaggatt ctgctaattc taataacttt cccagctggt agcagggaag catcgtatgt    336
cctttgtgtt tctcaaatct gcccaattgt tctctgcttt cggggaagct ttactcattt    396
tctaaaagaa atccaagtac tgtttggtca ttacccctta gtaaaaaaaa gtaacaggag    456
gatatcgtaa ttttctactg ttttattcct ctgttagacc gggccttgac atgaatgacg    516
ccgtaaggga gaaagagatc ttcccaatca gcaatcaccg taaaagcctg ctgtgttccc    576
gttaaaatta ggaaattctc actagatgaa ttgacatggg aggcatttag atttctaata    636
gtcacatagt aattctgcgg aggaattgag tcatctttga tagccatgga attaagcgat    696
gttaattaaa gtgcaaacga taacctttct gttcttacta gaatagagta ataaaaagaa    756
cctaggtttt cttttgtttg ctggaagaaa aatcaaaatt ctttagttct gtcaaaccag    816
aactcttgaa agcactttga acaatgcctg gaaaataaca ggtactctgt aaatgtttac    876
cttctctgca agtgcctgcc acgtgcccga agaaaagaca cattaaaaag ttaagtgaca    936
ccagtcctga ttttatatat tttatatacc taacaacgta tatgttagta tgtagaaatt    996
atatccttga ccttttttccc tacctattac gaactgtact tttattaaaa gctgccacta   1056
aaaaaaaaaa aaa                                                      1069
```

<210> 59
<211> 1084
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 135..818

<221> polyA_signal
<222> 909..914

<221> polyA_site
<222> 1071..1084

<400> 59
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cccactccgc tctcacgact aagctctcac gattaaggca cgcctgcctc gattgtccag     60
cctctgccag aagaaagctt agcagccagc gcctcagtag aggcctaagg gcgctgaatg    120
agtgggaaag ggaa atg ccg acc aat tgc gct gcg gcg ggc tgt gcc act      170
```

```
                Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr
                1               5                   10
acc tac aac aag cac att aac atc agc ttc cac agg ttt cct ttg gat      218
Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg Phe Pro Leu Asp
        15                  20                  25
cct aaa aga aga aaa gaa tgg gtt cgc ctg gtt agg cgc aaa aat ttt      266
Pro Lys Arg Arg Lys Glu Trp Val Arg Leu Val Arg Arg Lys Asn Phe
    30                  35                  40
gtg cca gga aaa cac act ttt ctt tgt tca aag cac ttt gaa gcc tcc      314
Val Pro Gly Lys His Thr Phe Leu Cys Ser Lys His Phe Glu Ala Ser
45                  50                  55                  60
tgt ttt gac cta aca gga caa act cga cga ctt aaa atg gat gct gtt      362
Cys Phe Asp Leu Thr Gly Gln Thr Arg Arg Leu Lys Met Asp Ala Val
                65                  70                  75
cca acc att ttt gat ttt tgt acc cat ata aag tct atg aaa ctc aag      410
Pro Thr Ile Phe Asp Phe Cys Thr His Ile Lys Ser Met Lys Leu Lys
            80                  85                  90
tca agg aat ctt ttg aag aaa aac aac agt tgt tct cca gct gga cca      458
Ser Arg Asn Leu Leu Lys Lys Asn Asn Ser Cys Ser Pro Ala Gly Pro
        95                  100                 105
tct agt tta aaa tca aac att agt agt cag caa gta cta ctt gaa cac      506
Ser Ser Leu Lys Ser Asn Ile Ser Ser Gln Gln Val Leu Leu Glu His
    110                 115                 120
agc tat gcc ttt agg aat cct atg gag gca aaa aag agg atc att aaa      554
Ser Tyr Ala Phe Arg Asn Pro Met Glu Ala Lys Lys Arg Ile Ile Lys
125                 130                 135                 140
ctg gaa aaa gaa ata gca agc tta aga aga aaa atg aaa act tgc cta      602
Leu Glu Lys Glu Ile Ala Ser Leu Arg Arg Lys Met Lys Thr Cys Leu
                145                 150                 155
caa aag gaa cgc aga gca act cga aga tgg atc aaa gcc atg tgt ttg      650
Gln Lys Glu Arg Arg Ala Thr Arg Arg Trp Ile Lys Ala Met Cys Leu
            160                 165                 170
gta aag aat tta gaa gca aat agt gta tta cct aaa ggt aca tca gaa      698
Val Lys Asn Leu Glu Ala Asn Ser Val Leu Pro Lys Gly Thr Ser Glu
        175                 180                 185
cac atg tta cca act gcc tta agc agt ctt cct ttg gaa gat ttt aag      746
His Met Leu Pro Thr Ala Leu Ser Ser Leu Pro Leu Glu Asp Phe Lys
    190                 195                 200
atc ctt gaa caa gat caa caa gat aaa aca ctg cta agt cta aat cta      794
Ile Leu Glu Gln Asp Gln Gln Asp Lys Thr Leu Leu Ser Leu Asn Leu
205                 210                 215                 220
aaa cag acc aag agt acc ttc att taaatttagc ttgcacagag cttgatgcct      848
Lys Gln Thr Lys Ser Thr Phe Ile
                225
atccttcatt cttttcagaa gtaaagataa ttatggcact tatgccaaaa ttcattattt      908
aataaagttt tacttgaagt aacattactg aatttgtgaa gacttgatta caaaagaata      968
aaaaacttca tatggaaatt ttatttgaaa atgagtggaa gcgccttaca ttagaattac     1028
ggacttaaaa attttgctaa taaattgtgt gtttgaaagg tgaaaaaaaa aaaaaa         1084
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<210> 60
<211> 419
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 33..290

<221> sig_peptide
<222> 33..92

<223> Von Heijne matrix
score 5.4
seq WFVHSSALGLVLA/PP

<400> 60
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aatggtaggc cttcatgtga gccagttact ac atg aat ctt cat ttc cca cag         53
                                    Met Asn Leu His Phe Pro Gln
                                    -20                 -15

tgg ttt gtt cat tca tca gcg tta ggc ttg gtc ctg gct cca cct ttc        101
Trp Phe Val His Ser Ser Ala Leu Gly Leu Val Leu Ala Pro Pro Phe
            -10                 -5                  1

tcc tct ccg ggc act gac ccc acc ttt ccg tgt att tac tgt agg cta        149
Ser Ser Pro Gly Thr Asp Pro Thr Phe Pro Cys Ile Tyr Cys Arg Leu
    5                   10                  15

tta aat atg atc atg acc cgc ctt gca ttt tca ttc atc acc tgt tta        197
Leu Asn Met Ile Met Thr Arg Leu Ala Phe Ser Phe Ile Thr Cys Leu
20                  25                  30                  35

tgc cca aat tta aag gaa gtt tgt ctc att ttg cca gaa aaa aat tgt        245
Cys Pro Asn Leu Lys Glu Val Cys Leu Ile Leu Pro Glu Lys Asn Cys
                40                  45                  50

aat agt cgg cac gct gga ttt gta ggg cca gca aaa ttg cgg cag            290
Asn Ser Arg His Ala Gly Phe Val Gly Pro Ala Lys Leu Arg Gln
            55                  60                  65

tgaaactagt ttcacttcta aagcccttca tttcccacaa ggttaagctc tcgaaacccc      350
atttgatcct tggttcctat ttcgatcctc ctttggaatc tgaaaatcgg tctccatgtt      410
gtatgcaaa                                                              419
```

<210> 61
<211> 682
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 485..616

<221> polyA_site
<222> 669..682

<400> 61
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ctcctttctc attccttatc ttgcgtgttt ttaccttttt ttcataacta agtttttgag       60
gaagttagtg ttcttttcaa agaaccggtt cgaaatgtac ttttctttgc tactttttgt      120
tattttattg atcacatctt taatcttttg ttctctatac gtggcctgtt ttgatttatt      180
ttactattct tgctttctaa ggtaagtatt ttgttgtgta gtgctttatt tttttcatct      240
ttcttcttga ataataatga catttttagg ttataaattt tcctctggta ctcagtttgc      300
ctcattaatt ttggcagtaa gcattctcct tttattgctt tctatgtagt ctttaatttt      360
gcttttaact tcttctttga tctaaggatt acctacttgt taatttccaa atattatctt      420
atctatctat ctatctatct atctatctat ctatctatct acctatgtga gacgaagtct      480
ggct atg tcg ccg agg ctg gag tgc agt ggt gca atc ttg gct cac tgc       529
     Met Ser Pro Arg Leu Glu Cys Ser Gly Ala Ile Leu Ala His Cys
     1               5                   10                  15

aac ccc cgc ctc cca ggt tca agt tat tct cct gcc tca gct act tgg        577
Asn Pro Arg Leu Pro Gly Ser Ser Tyr Ser Pro Ala Ser Ala Thr Trp
                20                  25                  30

gtg aga gga tcc ctt gag ccg ggg agg ttg agg ctg cag tgagccataa         626
Val Arg Gly Ser Leu Glu Pro Gly Arg Leu Arg Leu Gln
            35                  40

ccactactct ccagcctgga taacaaaagt gagactctga ccaaaaaaaa aaaaaa          682
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<210> 62
<211> 1191
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 54..995

<221> sig_peptide
<222> 54..227
<223> Von Heijne matrix
score 4.1
seq LVHHCPTWQWATG/EE

<221> polyA_signal
<222> 1130..1135

<221> polyA_site
<222> 1181..1191

<400> 62
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cacggctgca ctttccatcc cgtcgcgggg ccggccgcta ctccggcccc agg atg          56
                                                           Met
cag aat gtg att aat act gtg aag gga aag gca ctg gaa gtg gct gag        104
Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala Glu
        -55                 -50                 -45
tac ctg acc ccg gtc ctc aag gaa tca aag ttt agg gaa aca ggt gta        152
Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly Val
    -40                 -35                 -30
att acc cca gaa gag ttt gtg gca gct gga gat cac cta gtc cac cac        200
Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His His
-25                 -20                 -15                 -10
tgt cca aca tgg caa tgg gct aca ggg gaa gaa ttg aaa gtg aag gca        248
Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys Ala
                -5                  1               5
tac cta cca aca ggc aaa caa ttt ttg gta acc aaa aat gtg ccg tgc        296
Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro Cys
        10                  15                  20
tat aag cgg tgc aaa cag atg gaa tat tca gat gaa ttg gaa gct atc        344
Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala Ile
    25                  30                  35
att gaa gaa gat gat ggt gat ggc gga tgg gta gat aca tat cac aac        392
Ile Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His Asn
40                  45                  50                  55
aca ggt att aca gga ata acg gaa gcc gtt aaa gag atc aca ctg gaa        440
Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu Glu
                60                  65                  70
aat aag gac aat ata agg ctt caa gat tgc tca gca cta tgt gaa gag        488
Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu Glu
            75                  80                  85
gaa gaa gat gaa gat gaa gga gaa gct gca gat atg gaa gaa tat gaa        536
Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr Glu
        90                  95                  100
gag agt gga ttg ttg gaa aca gat gag gct acc cta gat aca agg aaa        584
Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg Lys
    105                 110                 115
ata gta gaa gct tgt aaa gcc aaa act gat gct ggc ggt gaa gat gct        632
Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp Ala
120                 125                 130                 135
att ttg caa acc aga act tat gac ctt tac atc act tat gat aaa tat        680
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```
Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys Tyr
                140                 145                 150
tac cag act cca cga tta tgg ttg ttt ggc tat gat gag caa cgg cag      728
Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg Gln
            155                 160                 165
cct tta aca gtt gag cac atg tat gaa gac atc agt cag gat cat gtg      776
Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His Val
        170                 175                 180
aag aaa aca gtg acc att gaa aat cat cct cat ctg cca cca cct ccc      824
Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro Pro
    185                 190                 195
atg tgt tca gtt cac cca tgc agg cat gct gag gtg atg aag aaa atc      872
Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys Ile
200                 205                 210                 215
att gag act gtt gca gaa gga ggg gga gaa ctt gga gtt cat atg tat      920
Ile Glu Thr Val Ala Glu Gly Gly Gly Glu Leu Gly Val His Met Tyr
                220                 225                 230
ctt ctt att ttc ttg aaa ttt gta caa gct gtc att cca aca ata gaa      968
Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile Glu
            235                 240                 245
tat gac tac aca aga cac ttc aca atg taatgaagag agcataaaat           1015
Tyr Asp Tyr Thr Arg His Phe Thr Met
        250                 255
ctatcctaat tattggttct gatttttaaa gaattaaccc atagatgtga ccattgacca   1075
tattcatcaa tatatacagt ttctctaata agggacttat atgtttatgc attaaataaa   1135
aatatgttcc actaccagcc ttacttgttt aataaaaatc agtgcaaaaa aaaaaa       1191
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<210> 63
<211> 1008
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 657..923

<221> sig_peptide
<222> 657..896
<223> Von Heijne matrix
      score 3.5
      seq RGLLSACAPWGDG/ST

<221> polyA_signal
<222> 957..962

<221> polyA_site
<222> 974..1008

<400> 63

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ntcgnatgtg gcacaaaacc cctctgctgg ctcatgtgtg caactgagac tgtcagagca     60
tggctagctc tggggtccag ctctgctggg tgggggctag agaggaagca gggagtatct    120
gcacacagga tgcctgcgct caggtggttg cagaagtcag tgcccaggcc cccccacaca    180
gtccccaaag gtccggcctc cccagcgcgg ggctcctcgt ttgaggggag gtgacttccc    240
tcccagcagg ctcttggaca cagtaagctt ccccagccct gcctgagcag cctttcctcc    300
ttgccctgtt ccccacctcc cggctccagt ccagggagct cccagggaag tggtcgaccc    360
ctccagtggc tgggccactc tgctagagtc catccgccaa gctgggggca tcggcaaggc    420
caagctgcgc agcatgaagg agcgaaagct ggagaagaag aagcagaagg agcaggagca    480
agtgagagcc acgagccaag gtgggcactt gatgtcggat ctcttcaaca agctggtcat    540
gaggcgcaag ggcatctctg ggaaagaacc tggggctggt gaggggcccg gaggagcctt    600
tgcccgcgtg tcagactcca tccctcctct gccgccaccg cagcagccac aggtag atg    659
```

```
                                                                  Met
                                                                  -80
agg aca agg acg act ggg aat cct agg ggg ctc cat gac acc ttc ccc      707
Arg Thr Arg Thr Thr Gly Asn Pro Arg Gly Leu His Asp Thr Phe Pro
                -75                 -70                 -65
cgc aga ccc aga ctt ggc cgt tgc tct gac atg gac aca gcc agg aca      755
Arg Arg Pro Arg Leu Gly Arg Cys Ser Asp Met Asp Thr Ala Arg Thr
            -60                 -55                 -50
agc tgc tca gac ctg ctt ccc tgg gag ggg gtg acg gaa cca gca ctg      803
Ser Cys Ser Asp Leu Leu Pro Trp Glu Gly Val Thr Glu Pro Ala Leu
        -45                 -40                 -35
tgt gga gac cag ctt caa gga acg gaa ggc tgg ctt gag gcc aca cag      851
Cys Gly Asp Gln Leu Gln Gly Thr Glu Gly Trp Leu Glu Ala Thr Gln
    -30                 -25                 -20
ctg ggg cgg gga ctt ctg tct gcc tgt gct cca tgg ggg gac ggc tcc      899
Leu Gly Arg Gly Leu Leu Ser Ala Cys Ala Pro Trp Gly Asp Gly Ser
-15                 -10                 -5                  1
acc cag cct gtg cca ctg tgt tct taagaggctt ccagagaaaa cggcacacca     953
Thr Gln Pro Val Pro Leu Cys Ser
            5
atcaataaag aactgagcag aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaan        1008
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<210> 64
<211> 568
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 18..311

<221> sig_peptide
<222> 18..62
<223> Von Heijne matrix
score 8.4
seq AMWLLCVALAVLA/WG

<400> 64

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agtgctgctt acccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg        50
                   Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu
                   -15                 -10                 -5
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga       98
Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg
                1               5                   10
atg aag agt cgg gag cag gga gga cgg ctg gga gcc gaa agc cgg acc      146
Met Lys Ser Arg Glu Gln Gly Gly Arg Leu Gly Ala Glu Ser Arg Thr
        15                  20                  25
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc      194
Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro
    30                  35                  40
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc      242
Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys
45                  50                  55                  60
ttc tct gca gtt ttc cgt agg gag cta agt gaa tac acc gaa ggt ctt      290
Phe Ser Ala Val Phe Arg Arg Glu Leu Ser Glu Tyr Thr Glu Gly Leu
                65                  70                  75
acc tct gaa ccc ctc aca gcc tagggacagg agcggccggc ttacctggtg         341
Thr Ser Glu Pro Leu Thr Ala
            80
ggttggggga cgtcggcagc tcgcgtacta cgccagcagg attgaggagc agagaaacag    401
```

```
ttgcagttgg ttgtattcag tacctgcatt tccgttggga actccacctg tacttgttat      461
tctgtggaac ttttttattt tgtagaagga gcaagaatat tgaccttact atatagcaca      521
cgaaacaatc tatgctgtat cgtgcctgct caatccttaa agttaac                    568



<210> 65
<211> 538
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 151..426

<221> sig_peptide
<222> 151..258
<223> Von Heijne matrix
      score 5.2
      seq KVALAGLLGFGLG/KV

<221> polyA_signal
<222> 505..510

<221> polyA_site
<222> 527..538

<400> 65
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat       60
catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag      120
caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc       174
                                 Met Leu Val Thr Gln Gly Leu Val
                                     -35                 -30
tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa        222
Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys
            -25                 -20                 -15
gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac        270
Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr
        -10                 -5                  1
ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt        318
Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg
5                   10                  15                  20
ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt        366
Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys
                25                  30                  35
gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag        414
Glu Glu Cys Lys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln
            40                  45                  50
cct tca gct tcc taaattctgt gtctgtgact ttcgaagttt tttaaacctc            466
Pro Ser Ala Ser
        55
tgaatttgta cacatttaaa atttcaagtg tactttaaaa taaaatactt ctaatggaac      526
aaaaaaaaaa aa                                                          538



<210> 66
<211> 1747
<212> DNA
<213> Homo sapiens

<220>
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<221> CDS
<222> 10..1062

<221> sig_peptide
<222> 10..57
<223> Von Heijne matrix
score 4.9
seq FIYLQAHFTLCSG/WS

<221> polyA_signal
<222> 1710..1715

<221> polyA_site
<222> 1735..1747

<400> 66
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gcctcacca atg gtt ccc ttc atc tat ctg caa gcc cac ttt aca ctc tgt      51
          Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys
              -15                 -10                 -5
tct ggg tgg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat gtg        99
Ser Gly Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val
        1               5                  10
ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg gta       147
Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val
15                  20                  25                  30
agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att gct gcc       195
Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala
                35                  40                  45
atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg gaa ggc       243
Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly
            50                  55                  60
atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc ccg       291
Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro
        65                  70                  75
gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac ctc       339
Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu
    80                  85                  90
ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct gaa       387
Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu
95                  100                 105                 110
gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac cac       435
Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His
                115                 120                 125
tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg gag tgg       483
Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp
            130                 135                 140
tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag gat ctg       531
Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu
        145                 150                 155
aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac agt       579
Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser
    160                 165                 170
ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca gtc       627
Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val
175                 180                 185                 190
aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gac ggt ttc       675
Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe
                195                 200                 205
tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct tgg       723
Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp
            210                 215                 220
aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc aac       771
```

```
Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn
        225                 230                 235
cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg cca gtg      819
Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val
    240                 245                 250
gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc tca      867
Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser
255                 260                 265                 270
cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag ggc ttc      915
Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe
                275                 280                 285
tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc agc      963
Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser
            290                 295                 300
gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc ccn     1011
Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro
        305                 310                 315
ttt tgt cac ctt gga cat gga aga ctg tgg cta caa cat tcc aca gac     1059
Phe Cys His Leu Gly His Gly Arg Leu Trp Leu Gln His Ser Thr Asp
    320                 325                 330
aga tgagtcaacc ctcatgacca tagcctatgt catggctgcc atctgcgccc          1112
Arg
335
tcttcatgct gccactctgc ctcatggtgt gtcagtggcg ctgcctccgc tgcctgcgcc   1172
agcagcatga tgactttgct gatgacatct ccctgctgaa gtgaggaggc ccatgggcag   1232
aagataggga ttcccctgga ccacacctcc gtggttcact ttggtcacaa gtaggagaca   1292
cagatggcac ctgtggccag agcacctcag gaccctcccc acccaccaaa tgcctctgcc   1352
ttgatggaga aggaaaaggc tggcaaggtg ggttccaggg actgtacctg taggagacag   1412
aaaagagaag aaagaagcac tctgctggcg ggaatactct tggtcacctc aaatttaagt   1472
cgggaaattc tgctgcttga aacttcagcc ctgaaccttt gtcaccattc ctttaaattc   1532
tccaacccaa agtattcttc ttttcttagt ttcagaagta ctggcatcac acgcaggtta   1592
ccttggcgtg tgtccctgtg gtaccctggc agagaagaga ccaagcttgt ttccctgctg   1652
gccaaagtca gtaggagagg atgcacagtt tgctatttgc tttagagaca gggactgtat   1712
aaacaagcct aacattggtg caaaaaaaaa aaaaa                              1747


&lt;210&gt; 67
&lt;211&gt; 1686
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; CDS
&lt;222&gt; 78..491

&lt;221&gt; sig_peptide
&lt;222&gt; 78..218
&lt;223&gt; Von Heijne matrix
      score 5.8
      seq LMCFGALIGLCAC/IC

&lt;221&gt; polyA_signal
&lt;222&gt; 1652..1657

&lt;221&gt; polyA_site
&lt;222&gt; 1673..1686

&lt;400&gt; 67
ggtatagccc accagaaagg acagagtcat ttgatgtggt cacaaaatgt gtgagtttca     60
cactaactga gcagttc atg gag aaa ttt gtt gat ccc gga aac cac aat       110
                   Met Glu Lys Phe Val Asp Pro Gly Asn His Asn
```

```
                                    -45                   -40
agc ggg att gat ctc ctt agg acc tat ctt tgg cgt tgc cag ttc ctt      158
Ser Gly Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu
    -35                 -30                   -25
tta cct ttt gtg agt tta ggt ttg atg tgc ttt ggg gct ttg atc gga      206
Leu Pro Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly
-20                 -15                 -10                 -5
ctt tgt gct tgc att tgc cga agc tta tat ccc acc att gcc acg ggc      254
Leu Cys Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly
                1               5                   10
att ctc cat ctc ctt gca ggt ctg tgt aca ctg ggc tca gta agt tgt      302
Ile Leu His Leu Leu Ala Gly Leu Cys Thr Leu Gly Ser Val Ser Cys
    15                  20                  25
tat gtt gct gga att gaa cta ctc cac cag aaa cta gag ctc cct gac      350
Tyr Val Ala Gly Ile Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp
    30                  35                  40
aat gta tcc ggt gaa ttt gga tgg tcc ttc tgc ctt gct tgt gtc tct      398
Asn Val Ser Gly Glu Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser
45                  50                  55                  60
gct ccc tta cag ttc atg gct tct gct ctc ttc atc tgg gct gct cac      446
Ala Pro Leu Gln Phe Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His
                65                  70                  75
acc aac cgg aga gag tac acc tta atg aag gca tat cgt gtg gca          491
Thr Asn Arg Arg Glu Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala
            80                  85                  90
tgagcaagaa actgcctgct ttacaattgc cattttttatt tttttaaaat aatactgata   551
ttttccccac ctctcaattg tttttaattt ttatttgtgg atataccatt ttattatgaa    611
aatctatttt atttatacac attcaccact aaatacacac ttaataccac taaaatttat    671
gtggtttact ttaagcgatg ccatctttca aataaactaa tctaggtcta gacagaaaga    731
aatggataga gacttgacac aaatttatga aagaaaattg ggagtaggaa tgtgaccgaa    791
aacaagttgt gctaatgtct gttagacttt tcagtaaaac caaagtaact gtatctgttc    851
aactaaaaac tctatattag tttctttggg aaacctctca tcgtcaaaac tttatgttca    911
ctttgctgtt gtagatagcc agtcaaccag cagtattagt gctgttttca aagatttaag    971
ctctataaaa ttgggaaatt atctaagatc attttcccta agcattgaca catagcttca   1031
tctgaggtga gatatggcag ctgtttgtat ctgcactgtg tctgtctaca aagagtgaaa   1091
aatacagtgt ttacttgaaa ttttaacttt gtaactgcaa gaattccagt tcggccgggc   1151
gaggattagt attattttta actctccgta agattttcag taccaccaaa ttgttttgga   1211
tttttttct ttcctcttca cataccaggg ttattaaaag tgtgctttct ttttacatta    1271
tattacagtt acaaggtaaa attcctcaac tgctatttat ttattccagc ccagtactat   1331
aaagaacgtt tcaccataat gaccctccag agctgggaaa cctaccacaa gatctaaagt   1391
tctggctgtc cattaacctc caactatggt ctttatttct tgtggtaata tgatgtgcct   1451
ttccttgcct aaatcccttc ctggtgtgta tcaacattat ttaatgtctt ctaattcagt   1511
catttttat aagtatgtct ataaacattg aactttaaaa aacttattta tttattccac    1571
tactgtagca attgacagat taaaaaaatg taacttcata atttcttacc ataacctcaa   1631
tgtcttttt aaaaaataaa attaaaaatg aaaagagacc caaaaaaaaa aaaaa         1686
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<210> 68
<211> 542
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 69..371

<221> sig_peptide
<222> 69..287
<223> Von Heijne matrix
score 4
seq AVGFLFWVIVLTS/WI

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<221> polyA_signal
<222> 510..515

<221> polyA_site
<222> 530..542

<400> 68
tgttacttag ggtcaaggct tgggtcttgc cccgcaaacc cttgggacga cccggcccca      60
gcgcagct atg aac ctg gag cga gtg tcc aat gag gag aaa ttg aac ctg      110
         Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu
                     -70                 -65                 -60
tgc cgg aag tac tac ctg ggg ggg ttt gct ttc ttg cct ttt ctc tgg      158
Cys Arg Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp
                -55                 -50                 -45
ttg gtc aac atc ttc tgg ttc tac cga gag gcc ttc ctt gtc cca gcc      206
Leu Val Asn Ile Phe Trp Phe Tyr Arg Glu Ala Phe Leu Val Pro Ala
            -40                 -35                 -30
tac aca gaa cag agc caa atc aaa ggc tat gtc tgg cgc tca gct gtg      254
Tyr Thr Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val
        -25                 -20                 -15
ggc ttc ctc ttc tgg gtg ata gtg ctc acc tcc tgg atc acc atc ttc      302
Gly Phe Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe
    -10                  -5                   1               5
cag atc tac cgg ccc cgc tgg ggt gcc ctt ggg gac tac ctc tcc ttc      350
Gln Ile Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe
                10                  15                  20
acc ata ccc ctg ggc acc ccc tgacaacttc tgcacatact ggggccctgc         401
Thr Ile Pro Leu Gly Thr Pro
            25
ttattctccc aggacaggct ccttaaagca gaggagcctg tcctgggagc cccttctcaa      461
actcctaaga cttgttctca tgtcccacgt tctctgctga catcccccaa taaaggaccc      521
taactttcaa aaaaaaaaaa a                                               542


<210> 69
<211> 1174
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..757

<221> sig_peptide
<222> 2..205
<223> Von Heijne matrix
      score 7.3
      seq LRLILSPLPGAQP/QQ

<221> polyA_site
<222> 1160..1174

<400> 69
g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag      49
  Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu
              -65                 -60                 -55
gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc      97
Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val
        -50                 -45                 -40
agc cgc aac cct gag gtg ccc ttt gag agc agt gcc tac cgc atc tca      145
```

```
Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser
    -35                 -30                 -25
gct tca gcc cgc ggc aag gag ctg cgc ctg ata ctg agc cct ctg cct      193
Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro
-20                 -15                 -10                 -5
ggg gcc cag cct caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc      241
Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly
                1               5                   10
atg tcc ggc tct ttt cag ctg gtg ccc cgc gag gag ctg cca cgc cat      289
Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His
        15                  20                  25
gcc cac ctg cgc ttt tac acg gcc ccg cct ggc ccc cgg ctc gcc cta      337
Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu
    30                  35                  40
tgt ttc gtg gac atc cgc cgg ttc ggc cgc tgg gac ctt ggg gga aag      385
Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys
45                  50                  55                  60
tgg cag ccg ggc cgc ggg ccc tgt gtc ttg cag gag tac cag cag ttc      433
Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe
                65                  70                  75
agg gag aat gtg cta cga aac cta gcg gat aag gcc ttt gac cgg ccc      481
Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro
            80                  85                  90
atc tgc gag gcc ctc ctg gac cag agg ttc ttc aat ggc att ggc aac      529
Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn
        95                  100                 105
tat ctg cgg gca gag atc ctg tac cgg ctg aag atc ccc ccc ttt gag      577
Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu
    110                 115                 120
aag gcc cgc tcg gtc ctg gag gcc ctg cag cag cac agg ccg agc ccg      625
Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro
125                 130                 135                 140
gag ctg acc ctg agc cag aag ata agg acc aag ctg cag aat tca gac      673
Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Ser Asp
                145                 150                 155
ctg ctg gag cta tgt cac tca gtg ccc aag gaa gtg gtc cag ttg ggt      721
Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly
            160                 165                 170
gag gcc aaa gat ggc agc aac ctc tgc ttc agc aaa tgattgtgta           767
Glu Ala Lys Asp Gly Ser Asn Leu Cys Phe Ser Lys
        175                 180
accctggggc acttgtcccc ctctggacct gattcaccga tttggaagtt tgtagcccta    827
gctgatactc aatggactag gcctcctcac ttgtcaatag tgtttccagg ctgggcgcag    887
tggctcatgc ctgtggtccc ggcacttcgg gaggccgagt ggggtggctc acctgaggtc    947
aggagttcga gaccatcctg gccaacatgg tgaaacccca tctccactaa aatgcaaaaa    1007
attagccagg tgtggtggcg ggcacctgta gtctcagcta ctcgggagga tgaggcagga    1067
aaatcgcttg aacccaggag gtggaggttg cagttgagct gagatcgtgc cattgcactc    1127
cagcctgggc aacgagagca aaactccatc tcaaaaaaaa aaaaaaa                  1174
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<210> 70
<211> 1285
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..1051

<221> sig_peptide
<222> 2..205
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<223> Von Heijne matrix
score 7.3
seq LRLILSPLPGAQP/QQ

<221> polyA_signal
<222> 1248..1253

<221> polyA_site
<222> 1272..1285

<400> 70
g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag 49
Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu
-65 -60 -55
gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc 97
Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val
-50 -45 -40
agc cgc aac cct gag gtg ccc ttt gag agc agt gcc tac cgc atc tca 145
Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser
-35 -30 -25
gct tca gcc cgc ggc aag gag ctg cgc ctg ata ctg agc cct ctg cct 193
Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro
-20 -15 -10 -5
ggg gcc cag ccc caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc 241
Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly
1 5 10
atg tcc ggc tct ttt cag ctg gtg ccc cgc gag gag ctg cca cgc cat 289
Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His
15 20 25
gcc cac ctg cgc ttt tac acg gcc ccg cct ggc ccc cgg ctc gcc cta 337
Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu
30 35 40
tgt ttc gtg gac atc cgc cgg ttc ggc cgc tgg gac ctt ggg gga aag 385
Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys
45 50 55 60
tgg cag ccg ggc cgc ggg ccc tgt gtc ttg cag gag tac cag cag ttc 433
Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe
65 70 75
agg ctg aag atc ccc ccc ttt gag aag gcc cgc tcg gtc ctg gag gcc 481
Arg Leu Lys Ile Pro Pro Phe Glu Lys Ala Arg Ser Val Leu Glu Ala
80 85 90
ctg cag cag cac agg ccg agc ccg gag ctg acc ctg agc cag aag ata 529
Leu Gln Gln His Arg Pro Ser Pro Glu Leu Thr Leu Ser Gln Lys Ile
95 100 105
agg acc aag ctg cag aat cca gac ctg ctg gag cta tgt cac tca gtg 577
Arg Thr Lys Leu Gln Asn Pro Asp Leu Leu Glu Leu Cys His Ser Val
110 115 120
ccc aag gaa gtg gac cag ttg ggg ggc agg ggc tac ggg tca gag agc 625
Pro Lys Glu Val Asp Gln Leu Gly Gly Arg Gly Tyr Gly Ser Glu Ser
125 130 135 140
ggg gag gag gac ttt gct gcc ttt cga gcc tgg ctg cgc tgc tat ggc 673
Gly Glu Glu Asp Phe Ala Ala Phe Arg Ala Trp Leu Arg Cys Tyr Gly
145 150 155
atg cca ggc atg agc tcc ctg cag gac cgg cat ggc cgt acc atc tgg 721
Met Pro Gly Met Ser Ser Leu Gln Asp Arg His Gly Arg Thr Ile Trp
160 165 170
ttc cag ggg gat cct gga ccg ttg gca ccc aaa ggg cgc aag tcc cgc 769
Phe Gln Gly Asp Pro Gly Pro Leu Ala Pro Lys Gly Arg Lys Ser Arg
175 180 185
aaa aag aaa tcc aag gcc aca cag ctg agt cct gag gac aga gtg gag 817
Lys Lys Lys Ser Lys Ala Thr Gln Leu Ser Pro Glu Asp Arg Val Glu
190 195 200

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gac gct ttg cct cca agc aag gcc cct tcc aag aca cga agg gca aag      865
Asp Ala Leu Pro Pro Ser Lys Ala Pro Ser Lys Thr Arg Arg Ala Lys
205                 210                 215                 220
aga gac ctt cct aag agg act gca acc cag cgg cct gag ggg acc agc      913
Arg Asp Leu Pro Lys Arg Thr Ala Thr Gln Arg Pro Glu Gly Thr Ser
                225                 230                 235
ctc cag cag gac cca gaa gct ccc aca gtg ccc aag aag ggg agg agg      961
Leu Gln Gln Asp Pro Glu Ala Pro Thr Val Pro Lys Lys Gly Arg Arg
            240                 245                 250
aag ggg cga cag gca gcc tct ggc cac tgc aga ccc cgg aag gtc aag     1009
Lys Gly Arg Gln Ala Ala Ser Gly His Cys Arg Pro Arg Lys Val Lys
        255                 260                 265
gct gac atc cca tcc ttg gaa cca gag ggg acc tca gcc tct             1051
Ala Asp Ile Pro Ser Leu Glu Pro Glu Gly Thr Ser Ala Ser
    270                 275                 280
tagcaggagg ctctccttgc ttgcactcac cctttcttat tgtcttgccc tgcatctggg   1111
ggtctgaatt tttgggagca ggcaatatct gaaggtgcaa acaggcccta cggctgttcc   1171
ctgcacaact ctcatggttt taattgtacc ccatcttcca catctttaaa gctcatgtga   1231
aaaatgctgc atttttaata aactgataca tttgaactcc aaaaaaaaaa aaaa         1285


<210> 71
<211> 1398
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..1171

<221> sig_peptide
<222> 2..205
<223> Von Heijne matrix
      score 7.3
      seq LRLILSPLPGAQP/QQ

<221> polyA_signal
<222> 1368..1373

<221> polyA_site
<222> 1386..1398

<400> 71
g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag     49
  Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu
              -65                 -60                 -55
gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc       97
Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val
        -50                 -45                 -40
agc cgc aac cct gag gtg ccc ttt gag agc agt gcc tac cgc atc tca      145
Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser
    -35                 -30                 -25
gct tca gcc cgc ggc aag gag ctg cgc ctg ata ctg agc cct ctg cct      193
Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro
-20                 -15                 -10                  -5
ggg gcc cag ccc caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc      241
Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly
                1               5                  10
atg tcc ggc tct ttt cag ctg gtg ccc cgc gag gag ctg cca cgc cat      289
Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His
        15                  20                  25
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gcc cac ctg cgc ttt tac acg gcc ccg cct ggc ccc cgg ctc gcc cta 337
Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu
30 35 40

tgt ttc gtg gac atc cgc cgg ttc ggc cgc tgg gac ctt ggg gga aag 385
Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys
45 50 55 60

tgg cag ccg ggc cgc ggg ccc tgt gtc ttg cag gag tac cag cag ttc 433
Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe
65 70 75

agg gag aat gtg cta cga aac cta gcg gat aag gcc ttt gac cgg ccc 481
Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro
80 85 90

atc tgc gag gcc ctc ctg gac cag agg ttc ttc aat ggc att ggc aac 529
Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn
95 100 105

tat ctg cgg gca gag atc ctg tac cgg ctg aag atc ccc ccc ttt gag 577
Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu
110 115 120

aag gcc cgc tcg gtc ctg gag gcc ctg cag cag cac agg ccg agc ccg 625
Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro
125 130 135 140

gag ctg acc ctg agc cag aag ata agg acc aag ctg cag aat cca gac 673
Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Pro Asp
145 150 155

ctg ctg gag cta tgt cac tca gtg ccc aag gaa gtg gtc cag ttg ggg 721
Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly
160 165 170

ggc aga ggc tac ggg tca gag agc ggg gag gag gac ttt gct gcc ttt 769
Gly Arg Gly Tyr Gly Ser Glu Ser Gly Glu Glu Asp Phe Ala Ala Phe
175 180 185

cga gcc tgg ctg cgc tgc tat ggc atg cca ggc atg agc tcc ctg cag 817
Arg Ala Trp Leu Arg Cys Tyr Gly Met Pro Gly Met Ser Ser Leu Gln
190 195 200

gac cgg cat ggc cgt acc atc tgg ttc cag ggg gat cct gga ccg ttg 865
Asp Arg His Gly Arg Thr Ile Trp Phe Gln Gly Asp Pro Gly Pro Leu
205 210 215 220

gca ccc aaa ggg cgc aag tcc cgc aaa aag aaa tcc aag gcc aca cag 913
Ala Pro Lys Gly Arg Lys Ser Arg Lys Lys Lys Ser Lys Ala Thr Gln
225 230 235

ctg agt cct gag gac aga gtg gag gac gct ttg cct ccg agc aag gcc 961
Leu Ser Pro Glu Asp Arg Val Glu Asp Ala Leu Pro Pro Ser Lys Ala
240 245 250

cct tcc agg aca cga agg gca aag aga gac ctt cct aag agg act gca 1009
Pro Ser Arg Thr Arg Arg Ala Lys Arg Asp Leu Pro Lys Arg Thr Ala
255 260 265

acc cag cgg cct gag ggg acc agc ctc cag cag gac cca gaa gct ccc 1057
Thr Gln Arg Pro Glu Gly Thr Ser Leu Gln Gln Asp Pro Glu Ala Pro
270 275 280

aca gtg ccc aag aag ggg agg agg aag ggg cga cag gca gcc tct ggc 1105
Thr Val Pro Lys Lys Gly Arg Arg Lys Gly Arg Gln Ala Ala Ser Gly
285 290 295 300

cac tgc aga ccc cgg aag gtc aag gct gac atc cca tcc ttg gaa cca 1153
His Cys Arg Pro Arg Lys Val Lys Ala Asp Ile Pro Ser Leu Glu Pro
305 310 315

gag ggg acc tca gcc tct tagcaggagg ctctccttgc ttgcactcac 1201
Glu Gly Thr Ser Ala Ser
320

cctttcttat tgtcttgccc tgcatctggg ggtctgaatt tttgggagca ggcaatatct 1261
gaaggtgcaa acaggcccta cggctgttcc ctgcacaact ctcatggttt taattgtacc 1321
ccatcttcca catctttaaa gctcatgtga aaaatgctgc atttttaata aactgataca 1381
tttgaaaaaa aaaaaaa 1398

<210> 72
<211> 821
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 42..611

<221> sig_peptide
<222> 42..287
<223> Von Heijne matrix
score 4.4
seq NLPHLQVVGLTWG/HI

<221> polyA_signal
<222> 787..792

<221> polyA_site
<222> 808..821

<400> 72
ccgttgccag ttctgcgcgt gtcctgcgtc tccagtatgg a atg tat gtt tgg ccc 56
Met Tyr Val Trp Pro
-80
tgt gct gtg gtc ctg gcc cag tac ctt tgg ttt cac aga aga tct ctg 104
Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe His Arg Arg Ser Leu
-75 -70 -65
cca ggc aag gcc atc tta gag att gga gca gga gtg agc ctt cca gga 152
Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly Val Ser Leu Pro Gly
-60 -55 -50
att ttg act gcc aaa tgt ggt gca gaa gta ata ctg tca gac agc tca 200
Ile Leu Thr Ala Lys Cys Gly Ala Glu Val Ile Leu Ser Asp Ser Ser
-45 -40 -35 -30
gaa ctg cct cac tgt ctg gaa gtc tgt cgg caa agc tgc caa atg aat 248
Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln Ser Cys Gln Met Asn
-25 -20 -15
aac ctg cca cat ctg cag gtg gta gga cta aca tgg ggt cat ata tct 296
Asn Leu Pro His Leu Gln Val Val Gly Leu Thr Trp Gly His Ile Ser
-10 -5 1
tgg gat ctt ctg gct cta cca cca caa gat att atc ctt gca tct gat 344
Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile Ile Leu Ala Ser Asp
5 10 15
gtg ttc ttt gaa cca gaa gat ttt gaa gac att ttg gct aca ata tat 392
Val Phe Phe Glu Pro Glu Asp Phe Glu Asp Ile Leu Ala Thr Ile Tyr
20 25 30 35
ttt ttg atg cac aag aat ccc aag gtc caa ttg tgg tct act tat caa 440
Phe Leu Met His Lys Asn Pro Lys Val Gln Leu Trp Ser Thr Tyr Gln
40 45 50
gtt agg agt gct gac tgg tca ctt gaa gct tta ctc tac aaa tgg gat 488
Val Arg Ser Ala Asp Trp Ser Leu Glu Ala Leu Leu Tyr Lys Trp Asp
55 60 65
atg aaa tgt gtc cac att cct ctt gag tct ttt gat gca gac aaa gaa 536
Met Lys Cys Val His Ile Pro Leu Glu Ser Phe Asp Ala Asp Lys Glu
70 75 80
gat ata gca gaa tct acc ctt cca gga aga cat aca gtt gaa atg ctg 584
Asp Ile Ala Glu Ser Thr Leu Pro Gly Arg His Thr Val Glu Met Leu
85 90 95
gtc att tcc ttt gca aag gac agt ctc tgaattatac ctacaacctg 631
Val Ile Ser Phe Ala Lys Asp Ser Leu

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100                 105
ttctgggaca gtatcaatac tgatgagcaa cctggcacac aaactatgag cagaccactt    691
cagcttgaga atgcagtggg tctgaagatg gtcaagtctg tctgccttag attttgatgt    751
cacctagaca acacttaaac tcatatgaaa caaaaattaa aatacgtatt acaagtaaaa    811
aaaaaaaaaa                                                           821
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<210> 73
<211> 916
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 62..916

<221> sig_peptide
<222> 62..757
<223> Von Heijne matrix
      score 4.2
      seq LVTPAALRPLVLG/GN

<221> polyA_site
<222> 904..916

<400> 73
cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct     60
g atg gga tgt gtt ttc cag agc aca gaa gac aaa cgt ata ttc aag ata    109
  Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Arg Ile Phe Lys Ile
          -230                -225                -220
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta      157
Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu
    -215                -210                -205
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc      205
Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg
-200                -195                -190                -185
gta cac ttg atg ggg gac aac tta tgc aat gat ggc tct ctc ctg ctc      253
Val His Leu Met Gly Asp Asn Leu Cys Asn Asp Gly Ser Leu Leu Leu
                -180                -175                -170
caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc      301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg
            -165                -160                -155
ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg      349
Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val
        -150                -145                -140
ctt cca gag gag ccc aaa gag ctc atg gtc cat gtg ggt gga ttg att      397
Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile
    -135                -130                -125
cag atg gga tgt gtt ttc cag agc aca gaa gtg aaa cac gtg acc aag      445
Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys
-120                -115                -110                -105
gta gaa tgg ata ttt tca gga cgg cgc gca aag gag gag att gta ttt      493
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Glu Glu Ile Val Phe
                -100                -95                 -90
cgt tac tac cac aaa ctc agg atg tct gcg gag tac tcc cag agc tgg      541
Arg Tyr Tyr His Lys Leu Arg Met Ser Ala Glu Tyr Ser Gln Ser Trp
            -85                 -80                 -75
ggc cac ttc cag aat cgt gtg aac ctg gtg ggg gac att ttc cgc aat      589
Gly His Phe Gln Asn Arg Val Asn Leu Val Gly Asp Ile Phe Arg Asn
        -70                 -65                 -60
gac ggt tcc atc atg ctt caa gga gtg agg gag tca gat gga gga aac      637
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Asp Gly Ser Ile Met Leu Gln Gly Val Arg Glu Ser Asp Gly Gly Asn
    -55                 -50                 -45
tac acc tgc agt atc cac cta ggg aac ctg gtg ttc aag aaa acc att      685
Tyr Thr Cys Ser Ile His Leu Gly Asn Leu Val Phe Lys Lys Thr Ile
-40                 -35                 -30                 -25
gtg ctg cat gtc agc ccg gaa gag cct cga aca ctg gtg acc ccg gca      733
Val Leu His Val Ser Pro Glu Glu Pro Arg Thr Leu Val Thr Pro Ala
                -20                 -15                 -10
gcc ctg agg cct ctg gtc ttg ggt ggt aat cag ttg gtg atc att gtg      781
Ala Leu Arg Pro Leu Val Leu Gly Gly Asn Gln Leu Val Ile Ile Val
            -5                  1               5
gga att gtc tgt gcc aca atc ctg ctg ctc cct gtc ctg ata ttg atc      829
Gly Ile Val Cys Ala Thr Ile Leu Leu Leu Pro Val Leu Ile Leu Ile
    10                  15                  20
gtg aag aag acc tgt gga aat aag agt tca gtg aat tct aca gtc ttg      877
Val Lys Lys Thr Cys Gly Asn Lys Ser Ser Val Asn Ser Thr Val Leu
25                  30                  35                  40
gtg aag aac acg aag aag act aat cca aaa aaa aaa aaa                  916
Val Lys Asn Thr Lys Lys Thr Asn Pro Lys Lys Lys Lys
                45                  50
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<210> 74
<211> 1153
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 62..520

<221> polyA_signal
<222> 1124..1129

<221> polyA_site
<222> 1141..1153

<400> 74

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cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct      60
g atg gga tgt gtt ttc cag agc aca gta gac aaa tgt ata ttc aag ata     109
  Met Gly Cys Val Phe Gln Ser Thr Val Asp Lys Cys Ile Phe Lys Ile
  1               5                   10                  15
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta      157
Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu
            20                  25                  30
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc      205
Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg
        35                  40                  45
gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc      253
Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu
    50                  55                  60
caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc      301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg
65                  70                  75                  80
ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg      349
Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val
                85                  90                  95
ctt cca gag gag ccc aaa gag ctc atg gtc cat gtg ggt gga ttg att      397
Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile
            100                 105                 110
cag atg gga tgt gtt ttc cag agc aca gaa gtg aaa cac gtg acc aag      445
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Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys
        115                 120                 125
gta gaa tgg ata ttt tca gga cgg cgc gca aag gta aca agg agg aaa      493
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Val Thr Arg Arg Lys
    130                 135                 140
cat cac tgt gtt aga gaa ggc tct ggc tgatggtatc aggacaaagg            540
His His Cys Val Arg Glu Gly Ser Gly
145                 150
tagaatcagg cacatgagga ggtgttgcaa gagcctgggc tttggtgctt atcagaactg    600
gaccttctcc tagcaatttc agctttctgg tgggaaaggt aactccaatg aagaacaaga    660
acaagaagat gatgatgatg cttaactttt tggatgccga tatgagattg tacatgtaaa    720
gcatttgta taagacttgg cccctgcatt ttagtttcct tctttctccc ttttccttcg     780
tatagagtcc atgggagaat gagggagatg atttttgtgg cccagccaag aaagcaatgg    840
gctagacatt aaaatgatta cacttttatt cttactgggg ttagttctgt gagttttcat    900
ctgtgcccca ttgccccatt tatgtgatgg agggaatttt catgggtact tcacgtgttg    960
ggattgattg atcctggggg ccagggtgaa gggtatttta cgggacctct ataaagcagg   1020
aagaagcaag tttattcttt agaccagtag ctctcaacca tgatgtggtc atatatttat   1080
gggtcaacat gtgttgtggg gatatcccaa gtaacttgtt attaataaaa gttaagttgc   1140
aaaaaaaaaa aaa                                                      1153
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<210> 75
<211> 1517
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 21..167

<400> 75

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ctctgaaatg cttgtctttt atg ctg gna ggt gac cat agg gct ctg ctt tta     53
                      Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu
                      1               5                   10
aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca      101
Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro
            15                  20                  25
ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct      149
Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro
        30                  35                  40
tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct             197
Ser Cys Pro Arg Phe Cys
    45
cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt    257
tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt    317
cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat    377
ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta    437
tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat    497
gcttgtcttt tatgctggga ggtgaccata gggctctgct tttaaagata tggctgcttc    557
aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag    617
ttaaaatgac ctcatgtcct tcttgtccac ggttttgttg agttttcact cttctaatgc    677
aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggcc aggaatgttg    737
aatgtctttg gctcagttca tttaaaaaag atatctattt gaaagttctc agagttgtac    797
atatgtttca cagtacagga tctgtacata aaagtttctt tcctaaacca ttcaccaaga    857
gccaatatct aggcattttc ttggtagcac aaattttctt attgcttaga aaattgtcct    917
ccttgttatt tctgtttgta agacttaagt gagttaggtc tttaaggaaa gcaacgctcc    977
tctgaaatgc ttgtctttna tgctgggagg tgaccatagg gctctgcttt taaagatatg   1037
gctgcttcaa aggccagagt cacaggaagg acttcttcca gggagattag tggtgatgga   1097
gaggagagtt aaaatgacct catgtccttc ttgtccacgg ttttgttgag ttttcactct   1157
tctaatgcaa gggtctcaca ctgtgaacca cttaggatgt gatcactttc aggtggccag   1217
gaatgttgaa tgtctttggc tcagttcatt taaaaaagat atctatttga aagttctcag   1277
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agttgtacat atgtttcaca gtacaggatc tgtacataaa agtttctttc ctaaaccatt 1337
caccaagagc caatatctag gcattttctt ggtagcacaa attttcttat tgcttagaaa 1397
attgtcctcc ttgttatttc tgtttgtaag acttaagtga gttaggtctt taaggaaagc 1457
aacgctcctc tgaaatgctt gtcttttatg ctgggaggtg accatagggc tctgctttta 1517

<210> 76
<211> 526
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 22..318

<221> sig_peptide
<222> 22..93
<223> Von Heijne matrix
score 4.6
seq FFIFCSLNTLLLG/GV

<221> polyA_signal
<222> 497..502

<221> polyA_site
<222> 516..526

<400> 76
ctgcctgctg cttgctgcac c atg aag tct gcc aag ctg gga ttt ctt cta 51
Met Lys Ser Ala Lys Leu Gly Phe Leu Leu
-20 -15
aga ttc ttc atc ttc tgc tca ttg aat acc ctg tta ttg ggt ggt gtt 99
Arg Phe Phe Ile Phe Cys Ser Leu Asn Thr Leu Leu Leu Gly Gly Val
-10 -5 1
aat aaa att gcg gag aag ata tgt gga gac ctc aaa gat ccc tgc aaa 147
Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp Pro Cys Lys
5 10 15
ttg gac atg aat ttt gga agc tgc tat gaa gtt cac ttt aga tat ttc 195
Leu Asp Met Asn Phe Gly Ser Cys Tyr Glu Val His Phe Arg Tyr Phe
20 25 30
tac aac aga acc tcc aaa aga tgt gaa act ttt gtc ttc tcc ggc tgt 243
Tyr Asn Arg Thr Ser Lys Arg Cys Glu Thr Phe Val Phe Ser Gly Cys
35 40 45 50
aat ggc aac ctt aac aac ttc aag ctt aaa ata gaa cgt gaa gta gcc 291
Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arg Glu Val Ala
55 60 65
tgt gtt gca aaa tac aaa cca ccg agg tgagaggatg tgaactcatg 338
Cys Val Ala Lys Tyr Lys Pro Pro Arg
70 75
aagttgtctg ctgcaccatc cgaaataaag acacaagaaa attcagactg attttgaaat 398
ctttgtaata tttccataat gctttaagct tccatatgtt tgctattttc ctgaccctag 458
ttttgtcttt cctggaaatt aactgtatga tcattagaat gaaagagtct ttctgtcaaa 518
aaaaaaaa 526

<210> 77
<211> 352
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS
<222> 8..292

<221> sig_peptide
<222> 8..118
<223> Von Heijne matrix
      score 5.6
      seq WLLLDALLRLGDT/KK

<221> polyA_signal
<222> 317..322

<221> polyA_site
<222> 339..352

<400> 77
ctgagat atg gca agt ccc gct gta aac agg tgg aaa agg cca agg ttg       49
        Met Ala Ser Pro Ala Val Asn Arg Trp Lys Arg Pro Arg Leu
                -35                 -30                 -25
aag ccg gtg tgg cca cgg cgc ttg gaa tcc tgg ttg ttg ctg gat gct       97
Lys Pro Val Trp Pro Arg Arg Leu Glu Ser Trp Leu Leu Leu Asp Ala
            -20                 -15                 -10
ctt ttg cga tta gga gat acc aaa aaa aag cga cag cct gaa gca gcc      145
Leu Leu Arg Leu Gly Asp Thr Lys Lys Lys Arg Gln Pro Glu Ala Ala
        -5                  1               5
aca aaa tcc tgt gtt aga agc agc tgt ggg ggt ccc agt gga gat ggg      193
Thr Lys Ser Cys Val Arg Ser Ser Cys Gly Gly Pro Ser Gly Asp Gly
10                  15                  20                  25
cct ccc cca tgc ctc cag cag cct gac cct cgt gcc ctg tct cag gcg      241
Pro Pro Pro Cys Leu Gln Gln Pro Asp Pro Arg Ala Leu Ser Gln Ala
                30                  35                  40
ttc tct aga tcc ttt cct ctg ttt ccc tct ctc gct ggc aaa agt atg      289
Phe Ser Arg Ser Phe Pro Leu Phe Pro Ser Leu Ala Gly Lys Ser Met
            45                  50                  55
atc taattgaaac aagactgaag gatcaataaa cagccatctg ccccttcaaa           342
Ile
aaaaaaaaaa                                                           352


<210> 78
<211> 542
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 16..378

<221> sig_peptide
<222> 16..84
<223> Von Heijne matrix
      score 9.8
      seq FLLFFFLFLLTRG/SL

<221> polyA_signal
<222> 502..507

<221> polyA_site
<222> 522..542
```

<400> 78
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cacgacctgt gggcc atg atg cta ccc caa tgg ctg ctg ctg ctg ttc ctt       51
                 Met Met Leu Pro Gln Trp Leu Leu Leu Leu Phe Leu
                             -20                     -15
ctc ttc ttc ttt ctc ttc ctc ctc acc agg ggc tca ctt tct cca aca        99
Leu Phe Phe Phe Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr
    -10                 -5                  1               5
aaa tat aac ctt ttg gag ctc aag gag tct tgc atc cgg aac cag gac       147
Lys Tyr Asn Leu Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp
                10                  15                  20
tgc gag act ggc tgc tgc caa cgt gct cca gac aat tgc gag tcg cac       195
Cys Glu Thr Gly Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His
            25                  30                  35
tgc gcg gag aag ggg tcc gag ggc agt ctg tgt caa acg cag gtg ttc       243
Cys Ala Glu Lys Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe
        40                  45                  50
ttt ggc caa tat aga gcg tgt ccc tgc ctg cgg aac ctg act tgt ata       291
Phe Gly Gln Tyr Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile
    55                  60                  65
tat tca aag aat gag aaa tgg ctt agc atc gcc tat ggc cgt tgt cag       339
Tyr Ser Lys Asn Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln
70                  75                  80                  85
aaa att gga agg cag aag ttg gct aag aaa atg ttc ttc tagtgctccc        388
Lys Ile Gly Arg Gln Lys Leu Ala Lys Lys Met Phe Phe
                90                  95
tccttcttgc tgcctcctcc tcctccacct gctctcctcc ctacccagag ctctgtgttc     448
accctgttcc ccagagcctc caccatgagt ggagggaagt ggggagtgat tgaaataaag     508
agctttttca atgaaaaaaa aaaaaaaaaa aaaa                                 542
```

<210> 79
<211> 233
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 57..233

<400> 79
```
gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg      59
                                                              Met
                                                              1
atc cta tgt ttc ctt ctt cct cat cat cgt ctt cag gaa gcc aga cag       107
Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg Gln
            5                   10                  15
att caa gta ttg aag atg ctg cca agg gaa aaa tta aga aga aga gaa       155
Ile Gln Val Leu Lys Met Leu Pro Arg Glu Lys Leu Arg Arg Arg Glu
        20                  25                  30
gag aga aaa caa ata aat ggg aaa aaa gaa agg aca aaa tat gaa aca       203
Glu Arg Lys Gln Ile Asn Gly Lys Lys Glu Arg Thr Lys Tyr Glu Thr
    35                  40                  45
cca aga aaa aga gaa gga aaa aaa aaa aaa                               233
Pro Arg Lys Arg Glu Gly Lys Lys Lys Lys
50                  55
```

<210> 80
<211> 660
<212> DNA

<213> Homo sapiens

<220>
<221> CDS
<222> 83..340

<221> sig_peptide
<222> 83..124
<223> Von Heijne matrix
      score 7.5
      seq VALNLILVPCCAA/WC

<221> polyA_signal
<222> 573..578

<221> polyA_site
<222> 607..660

<400> 80
```
gaatttgtaa aacttctgct cgtttacact gcacattgaa tacaggtaac taattggaag      60
gagaggggag atcactcttt tg atg gtg gcc ctg aac ctc att ctg gtt ccc     112
                         Met Val Ala Leu Asn Leu Ile Leu Val Pro
                                             -10                 -5
tgc tgc gct gct tgg tgt gac cca cgg agg atc cac tcc cag gat gac      160
Cys Cys Ala Ala Trp Cys Asp Pro Arg Arg Ile His Ser Gln Asp Asp
                1               5                   10
gtg ccc cgt agc tct gct gct gat act ggg tct gcg atg cag cgg cgt      208
Val Pro Arg Ser Ser Ala Ala Asp Thr Gly Ser Ala Met Gln Arg Arg
        15                  20                  25
gag gcc tgg gct ggt tgg aga agg tca caa ccc ttc tct gtt ggt ctg      256
Glu Ala Trp Ala Gly Trp Arg Arg Ser Gln Pro Phe Ser Val Gly Leu
    30                  35                  40
cct tct gct gaa aga ctc gag aac caa cca ggg aag ctg tcc tgg agg      304
Pro Ser Ala Glu Arg Leu Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg
45                  50                  55                  60
tcc ctg gtc gga gag gga tat aga atc tgt gac ctc tgacaactgt           350
Ser Leu Val Gly Glu Gly Tyr Arg Ile Cys Asp Leu
                65                  70
gaagccaccc tgggctacag aaaccacagt cttcccagca attattacaa ttcttgaatt   410
ccttggggat tttttactgc cctttcaaag cacttaagtg ttagatctaa cgtgttccag   470
tgtctgtctg aggtgactta aaaaatcaga acaaaacttc tattatccag agtcatggga   530
gagtacaccc tttccaggaa taatgttttg ggaaacactg aaatgaaatc ttcccagtat   590
tataaattgt gtatttaaaa aaagaaactt ttctgaatgc ctacctggcg gtgtatacca   650
ggcagtgtgc                                                          660
```

<210> 81
<211> 605
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 47..541

<221> sig_peptide
<222> 47..220
<223> Von Heijne matrix
      score 5.4
      seq QLLDSVLWLGALG/LT

<221> polyA_site
<222> 597..605

<400> 81
```
aaagtgggag gagcactagg tcttcccgtc acctccacct ctctcc atg acc cgg         55
                                                   Met Thr Arg
ctc tgc tta ccc aga ccc gaa gca cgt gag gat ccg atc cca gtt cct       103
Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile Pro Val Pro
-55                 -50                 -45                 -40
cca agg ggc ctg ggt gct ggg gag ggg tca ggt agt cca gtg cgt cca       151
Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro Val Arg Pro
                -35                 -30                 -25
cct gta tcc acc tgg ggc cct agc tgg gcc cag ctc ctg gac agt gtc       199
Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu Asp Ser Val
            -20                 -15                 -10
cta tgg ctg ggg gca cta gga ctg aca atc cag gca gtc ttt tcc acc       247
Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val Phe Ser Thr
        -5                  1               5
act ggc cca gcc ctg ctg ctg ctt ctg gtc agc ttc ctc acc ttt gac       295
Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe Leu Thr Phe Asp
10                  15                  20                  25
ctg ctc cat agg ccc gca ggt cac act ctg cca cag cgc aaa ctt ctc       343
Leu Leu His Arg Pro Ala Gly His Thr Leu Pro Gln Arg Lys Leu Leu
                30                  35                  40
acc agg ggc cag agt cag ggg gcc ggt gaa ggt cct gga cag cag gag       391
Thr Arg Gly Gln Ser Gln Gly Ala Gly Glu Gly Pro Gly Gln Gln Glu
            45                  50                  55
gct cta ctc ctg caa atg ggt aca gtc tca gga caa ctt agc ctc cag       439
Ala Leu Leu Leu Gln Met Gly Thr Val Ser Gly Gln Leu Ser Leu Gln
        60                  65                  70
gac gca ctg ctg ctg ctg ctc atg ggg ctg ggc ccg ctc ctg aga gcc       487
Asp Ala Leu Leu Leu Leu Leu Met Gly Leu Gly Pro Leu Leu Arg Ala
    75                  80                  85
tgt ggc atg ccc ttg acc ctg ctt ggc ctg gct ttc tgc ctc cat cct       535
Cys Gly Met Pro Leu Thr Leu Leu Gly Leu Ala Phe Cys Leu His Pro
90                  95                  100                 105
tgg gcc tgagagcccc tccccacaac tcagtgtcct tcaaatatac aatgaccacc        591
Trp Ala
cttcttcaaa aaaa                                                       605
```

<210> 82
<211> 396
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..285

<221> sig_peptide
<222> 46..150
<223> Von Heijne matrix
score 3.6
seq LEPGLSSSAACNG/KE

<221> polyA_signal
<222> 364..369

<221> polyA_site
<222> 385..396

<400> 82
cctctacagg aatcagactc agcctctttt ggttttcagt gaagt atg cct ttt caa 57
Met Pro Phe Gln
-35
ttt gga acc cag cca agg agg ttt cca gtg gaa gga gga gat tct tca 105
Phe Gly Thr Gln Pro Arg Arg Phe Pro Val Glu Gly Gly Asp Ser Ser
-30 -25 -20
att gag ctg gaa cct ggg ctg agc tcc agt gct gcc tgt aat ggg aag 153
Ile Glu Leu Glu Pro Gly Leu Ser Ser Ser Ala Ala Cys Asn Gly Lys
-15 -10 -5 1
gag atg tca cca acc agg caa ctc cgg agg tgc cct gga agt cat tgc 201
Glu Met Ser Pro Thr Arg Gln Leu Arg Arg Cys Pro Gly Ser His Cys
5 10 15
ctg aca ata act gat gtt ccc gtc act gtt tat gca aca acg aga aag 249
Leu Thr Ile Thr Asp Val Pro Val Thr Val Tyr Ala Thr Thr Arg Lys
20 25 30
cca cct gca caa agc agc aag gaa atg cat cct aaa tagcaccatt 295
Pro Pro Ala Gln Ser Ser Lys Glu Met His Pro Lys
35 40 45
aagtcttttg tcaaggtctg actaggtcaa gggtaatgga ccagtatcat ctggtgatct 355
ggtaaacaaa taaaagtggt ggcaccttca aaaaaaaaaa a 396

<210> 83
<211> 432
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 22..240

<221> sig_peptide
<222> 22..84
<223> Von Heijne matrix
score 12
seq VLVLCVLLLQAQG/GY

<221> polyA_signal
<222> 397..402

<221> polyA_site
<222> 421..432

<400> 83
gctcacgctc tggtcagagt t atg gca ccc cag act ctg ctg cct gtc ctg 51
Met Ala Pro Gln Thr Leu Leu Pro Val Leu
-20 -15
gtt ctc tgt gtg ctg ctg ctg cag gcc cag gga gga tac cgt gac aag 99
Val Leu Cys Val Leu Leu Leu Gln Ala Gln Gly Gly Tyr Arg Asp Lys
-10 -5 1 5
atg agg atg cag aga atc aag gtc tgt gag aag cga ccc agc ata gat 147
Met Arg Met Gln Arg Ile Lys Val Cys Glu Lys Arg Pro Ser Ile Asp
10 15 20
cta tgc atc cac cac tgt tca tgt ttc caa aag tgt gaa aca aat aag 195
Leu Cys Ile His His Cys Ser Cys Phe Gln Lys Cys Glu Thr Asn Lys
25 30 35
ata tgc tgt tca gcc ttc tgt ggg aac att tgt atg agc atc cta 240
Ile Cys Cys Ser Ala Phe Cys Gly Asn Ile Cys Met Ser Ile Leu
40 45 50

```
tgagtgggag agtgggctgg gatgtgcatc ctgctccctg aacccttcca tccgagactg     300
tgcccacatc cgaagcacaa ggacatcaaa tcatcagcac aagaacatca acaggaatgc     360
caccctcccc agtgtctgaa ctccctgtcc ctgtcaaatg aaccagaaca aatgcccatg     420
aaaaaaaaaa aa                                                         432



<210> 84
<211> 420
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 89..382

<221> polyA_site
<222> 408..420

<400> 84
gcttgcctga cccccatgtc gcctctgtag gtagaagaag tatgtcttcc tggacccccct     60
ggctggtgct gtaacaaaga cccatgtg atg ctg ggg gca gag aca gag gag       112
                               Met Leu Gly Ala Glu Thr Glu Glu
                               1               5
aag ctg ttt gat gcc ccc ttg tcc atc agc aag aga gag cag ctg gaa      160
Lys Leu Phe Asp Ala Pro Leu Ser Ile Ser Lys Arg Glu Gln Leu Glu
    10                  15                  20
cag cag gtc cca gag aac tac ttc tat gtg cca gac ctg ggc cag gtg      208
Gln Gln Val Pro Glu Asn Tyr Phe Tyr Val Pro Asp Leu Gly Gln Val
25                  30                  35                  40
cct gag att gat gtt cca tcc tac ctg cct gac ctg ccc ggc att gcc      256
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala
                45                  50                  55
aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct      304
Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser
            60                  65                  70
gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc      352
Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala
        75                  80                  85
gag cct ctc aag acc tac aag atg ggg tac taacagcacc accaccgccc        402
Glu Pro Leu Lys Thr Tyr Lys Met Gly Tyr
    90                  95
ccaccaaaaa aaaaaaaa                                                  420



<210> 85
<211> 501
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 80..415

<221> sig_peptide
<222> 80..142
<223> Von Heijne matrix
      score 5.4
      seq TFCLIFGLGAVWG/LG

<221> polyA_signal
```

<222> 471..476

<221> polyA_site
<222> 488..501

<400> 85
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cccgcttgat tccaagaacc tcttcgatat ttatttttat ttttaaagag ggagacgatg     60
gactgagctg atccgcacc atg gag tct cgg gtc tta ctg aga aca ttc tgt    112
                     Met Glu Ser Arg Val Leu Leu Arg Thr Phe Cys
                             -20                 -15
ttg atc ttc ggt ctc gga gca gtt tgg ggg ctt ggt gtg gac cct tcc    160
Leu Ile Phe Gly Leu Gly Ala Val Trp Gly Leu Gly Val Asp Pro Ser
-10                 -5                  1               5
cta cag att gac gtc tta aca gag tta gaa ctt ggg gag tcc acg acc    208
Leu Gln Ile Asp Val Leu Thr Glu Leu Glu Leu Gly Glu Ser Thr Thr
            10                  15                  20
gga gtg cgt cag gtc ccg ggg ctg cat aat ggg acg aaa gcc ttt ctc    256
Gly Val Arg Gln Val Pro Gly Leu His Asn Gly Thr Lys Ala Phe Leu
        25                  30                  35
ttt caa gat act ccc aga agc ata aaa gca tcc act gct aca gct gaa    304
Phe Gln Asp Thr Pro Arg Ser Ile Lys Ala Ser Thr Ala Thr Ala Glu
    40                  45                  50
cag ttt ttt cag aag ctg aga aat aaa cat gaa ttt act att ttg gtg    352
Gln Phe Phe Gln Lys Leu Arg Asn Lys His Glu Phe Thr Ile Leu Val
55                  60                  65                  70
acc cta aaa cag acc cac tta aat tca gga gtt att ctc tca att cac    400
Thr Leu Lys Gln Thr His Leu Asn Ser Gly Val Ile Leu Ser Ile His
                75                  80                  85
cac ttg gat cac agg taaatgtggt tgctggagtt tcctgtgttt tcattatatg    455
His Leu Asp His Arg
            90
tggttaaatg aatatattaa agagaagtaa acaaaaaaaa aaaaaa                  501
```

<210> 86
<211> 454
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 152..361

<221> sig_peptide
<222> 152..283
<223> Von Heijne matrix
score 4.7
seq FLLSLSLITYCFW/DP

<400> 86
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gacattttac ttttttctgt taacgcttac cctagaaatt agaaatgaca ccacgtattc     60
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac    120
gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata       172
                                   Met Cys Cys Tyr Cys Arg Ile
                                                      -40
ttt tgt ctt aga tgt acg tac ttt cct gtt cat tgt ggt atg tgt aat    220
Phe Cys Leu Arg Cys Thr Tyr Phe Pro Val His Cys Gly Met Cys Asn
        -35                 -30                 -25
ttg cgt tac ttt gaa ttt tcc acg ttt tta ctt tct ttg tct ctc atc    268
Leu Arg Tyr Phe Glu Phe Ser Thr Phe Leu Leu Ser Leu Ser Leu Ile
    -20                 -15                 -10
```

act tac tgc ttt tgg gac ccc ccc cat cgg ggt tca cat tcc ctc tcc 316
Thr Tyr Cys Phe Trp Asp Pro Pro His Arg Gly Ser His Ser Leu Ser
-5 1 5 10
cta gag cac act ccc ttg gat ttc ctc gag tgg ggt ctg ctg cgg 361
Leu Glu His Thr Pro Leu Asp Phe Leu Glu Trp Gly Leu Leu Arg
15 20 25
tgaagctttc ccattttatg tgcagattat tttcagaggg tatatagaat tcaggcagct 421
gtttcgttgt agcacattaa aaatattttc ccc 454

<210> 87
<211> 1272
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 32..307

<221> sig_peptide
<222> 32..70
<223> Von Heijne matrix
score 4.2
seq MLFSLSLLSNLNQ/IG

<221> polyA_signal
<222> 1240..1245

<221> polyA_site
<222> 1261..1272

<400> 87
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt 52
Met Leu Phe Ser Leu Ser Leu
-10
ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac 100
Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His
-5 1 5 10
att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa 148
Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln
15 20 25
caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac 196
Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His
30 35 40
aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa 244
Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys
45 50 55
cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca 292
Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser
60 65 70
cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctct 347
Pro Phe Leu Ala Cys
75
cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcgggag 407
agaaatcaca agccgtcccg atccttctct aggtctcgta gtcgatttag gtcaaatgaa 467
aggaaataga agacagtttg caagagaagt ggtgtacagg aaattacttc atttgacagg 527
agtatgtaca gaaaattcaa gttttgtttg agacttcata agcttggtgc atttttaaga 587
tgttttagct gttcaaatct gtttgtctct tgaaacagtg acacaaaagt gtaattctct 647
atggtttgaa atggatcata cgaggcatgt aataccaaga attgttactt tacaatgttc 707
ccttaagcaa aattgaattt gctttgaact tttagttatg cacagactga taataaacct 767
ctaaacctgc ccagcggaag tgtgtttttt tttaaattta aatacagaaa caactggcaa 827

aaattgaact aagatttact tttttttcca tagctgggat ataggctgca gctatagttg 887
aacaagcagt ctttaaaaac tgctgtgaaa cacaggccat cagggaaaac gaaatgctgc 947
actattaaat tagaggtttt tgaaaaatcc aactctcatc ctgggcagag gttgcctagt 1007
tggtatagaa tgttaagttt caagaaagtt tacctttgct ttaggtcgta agttccttat 1067
ttgattgccg tatatggata catggctgtt cgtgacattc tttatgtgca aatttgtgat 1127
ttcaaaaatg tcctgccagt ttaagggtac attgtagagc cgaactttga gttactgtgc 1187
aagatttttt ttcatgctgt catttgtaat atgttttgtg agaatccttg ggattaaagt 1247
tttggttaca gattaaaaaa aaaaa 1272

<210> 88
<211> 804
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 114..734

<221> sig_peptide
<222> 114..239
<223> Von Heijne matrix
score 5.2
seq LLFDLVCHEFCQS/DD

<221> polyA_signal
<222> 768..773

<221> polyA_site
<222> 793..804

<400> 88
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgccct gtatacttga 60
agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg 116
Met

cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att 164
His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile
-40 -35 -30

gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac 212
Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp
-25 -20 -15 -10

ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt 260
Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu
-5 1 5

caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc 308
Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala
10 15 20

atc tat gcc tca cag act gag caa gag tat cta aag ata gaa aaa gta 356
Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val
25 30 35

gat ctt cct cta att gac agc ctc att cgg gtc tta caa aat atg gaa 404
Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met Glu
40 45 50 55

cag tgt cag aaa aaa cca gag aac tcg gca gag tct aac aca gag gaa 452
Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu Glu
60 65 70

act aaa agg act gat tta acc caa gat gat ctc cac ttg aaa atc tta 500
Thr Lys Arg Thr Asp Leu Thr Gln Asp Asp Leu His Leu Lys Ile Leu
75 80 85

aag gat att tta tgt gaa ttt ctt tct aat att ttt cag gca tta aca 548
Lys Asp Ile Leu Cys Glu Phe Leu Ser Asn Ile Phe Gln Ala Leu Thr

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        90                  95                  100
aag gag acg gtg gct cag gga gta aag gaa ggc cag ttg agc aaa cag      596
Lys Glu Thr Val Ala Gln Gly Val Lys Glu Gly Gln Leu Ser Lys Gln
    105                 110                 115
aag tgt tcc tct gca ttt caa aac ctt ctt cct ttc tat agc cct gtg      644
Lys Cys Ser Ser Ala Phe Gln Asn Leu Leu Pro Phe Tyr Ser Pro Val
120                 125                 130                 135
gtg gaa gat ttt att aaa atc cta cgt gaa gtt gat aag gcg ctt gct      692
Val Glu Asp Phe Ile Lys Ile Leu Arg Glu Val Asp Lys Ala Leu Ala
                140                 145                 150
gat gac ttg gaa aaa aac ttc cca agt ttg aag gtt cag act              734
Asp Asp Leu Glu Lys Asn Phe Pro Ser Leu Lys Val Gln Thr
            155                 160                 165
taaaacctga attggaatta cttctgtaca agaaataaac tttatttttc tcactgacaa    794
aaaaaaaaaa                                                           804



<210> 89
<211> 802
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 199..801

<221> polyA_signal
<222> 780..785

<221> polyA_site
<222> 791..802

<400> 89
agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaagag     60
gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttacga    120
tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtggcc    180
tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc      231
                    Met Gln Val Ala Leu Lys Glu Asp Leu Asp Ala
                    1               5                   10
ctc aag gaa aaa ttt cga aca atg gaa tct aat cag aaa agc tca ttc      279
Leu Lys Glu Lys Phe Arg Thr Met Glu Ser Asn Gln Lys Ser Ser Phe
            15                  20                  25
caa gaa atc ccc aaa ctt aat gaa gaa cta ctc agc aag caa aaa caa      327
Gln Glu Ile Pro Lys Leu Asn Glu Glu Leu Leu Ser Lys Gln Lys Gln
        30                  35                  40
ctt gag aag att gaa tct gga gag atg ggt ttg aac aaa gtc tgg ata      375
Leu Glu Lys Ile Glu Ser Gly Glu Met Gly Leu Asn Lys Val Trp Ile
    45                  50                  55
aac atc aca gaa atg aat aag cag att tct ctg ttg act tct gca gtg      423
Asn Ile Thr Glu Met Asn Lys Gln Ile Ser Leu Leu Thr Ser Ala Val
60                  65                  70                  75
aac cac ctc aaa gcc aat gtt aag tca gct gca gac ttg att agc ctg      471
Asn His Leu Lys Ala Asn Val Lys Ser Ala Ala Asp Leu Ile Ser Leu
                80                  85                  90
cct acc act gta gag gga ctt cag aag agt gta gct tcc att ggc aat      519
Pro Thr Thr Val Glu Gly Leu Gln Lys Ser Val Ala Ser Ile Gly Asn
            95                  100                 105
act tta aac agc gtc cat ctt gct gtg gaa gca cta cag aaa act gtg      567
Thr Leu Asn Ser Val His Leu Ala Val Glu Ala Leu Gln Lys Thr Val
        110                 115                 120
gat gaa cac aag aaa acg atg gaa tta ctg cag agt gat atg aat cag      615
```

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Asp Glu His Lys Lys Thr Met Glu Leu Leu Gln Ser Asp Met Asn Gln
    125                 130                 135
cac ttc ttg aag gag act cct gga agc aac cag atc att ccg tca cct      663
His Phe Leu Lys Glu Thr Pro Gly Ser Asn Gln Ile Ile Pro Ser Pro
140                 145                 150                 155
tca gcc aca tca gaa ctt gac aat aaa acc cac agt gag aat ttg aaa      711
Ser Ala Thr Ser Glu Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys
                160                 165                 170
cag atg ggt gat aga tct gcc act ctg aaa aga cag tct ttg gac caa      759
Gln Met Gly Asp Arg Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln
            175                 180                 185
gtc acc aac aga aca gat aca gta aaa atc caa aaa aaa aaa a            802
Val Thr Asn Arg Thr Asp Thr Val Lys Ile Gln Lys Lys Lys
        190                 195                 200
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<210> 90
<211> 1490
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 38..1174

<221> sig_peptide
<222> 38..148
<223> Von Heijne matrix
score 7.3
seq LLSACLVTLWGLG/EP

<221> polyA_signal
<222> 1452..1457

<221> polyA_site
<222> 1478..1490

<400> 90

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tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg      55
                                         Met Pro His Ser Ser Leu
                                                     -35
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc      103
His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala
    -30                 -25                 -20
ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag      151
Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu
-15                 -10                 -5                  1
cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg      199
Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu
            5                   10                  15
cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg      247
Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu
        20                  25                  30
cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg      295
Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg
    35                  40                  45
gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg ctg tcc      343
Ala Cys Leu Gly Cys Pro Leu Arg Arg Gly Ala Leu Leu Leu Leu Ser
50                  55                  60                  65
atc tat ttc tac tac tcc ctc cca aat gcg gtc ggc ccg ccc ttc act      391
Ile Tyr Phe Tyr Tyr Ser Leu Pro Asn Ala Val Gly Pro Pro Phe Thr
```

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                    70                     75                     80
tgg atg ctt gcc ctc ctg ggc ctc tcg cag gca ctg aac atc ctc ctg      439
Trp Met Leu Ala Leu Leu Gly Leu Ser Gln Ala Leu Asn Ile Leu Leu
                85                     90                     95
ggc ctc aag ggc ctg gcc cca gct gag atc tct gca gtg tgt gaa aaa      487
Gly Leu Lys Gly Leu Ala Pro Ala Glu Ile Ser Ala Val Cys Glu Lys
            100                    105                    110
ggg aat ttc aac gtg gcc cat ggg ctg gca tgg tca tat tac atc gga      535
Gly Asn Phe Asn Val Ala His Gly Leu Ala Trp Ser Tyr Tyr Ile Gly
        115                    120                    125
tat ctg cgg ctg atc ctg cca gag ctc cag gcc cgg att cga act tac      583
Tyr Leu Arg Leu Ile Leu Pro Glu Leu Gln Ala Arg Ile Arg Thr Tyr
    130                    135                    140                    145
aat cag cat tac aac aac ctg cta cgg ggt gca gtg agc cag cgg ctg      631
Asn Gln His Tyr Asn Asn Leu Leu Arg Gly Ala Val Ser Gln Arg Leu
                    150                    155                    160
tat att ctc ctc cca ttg gac tgt ggg gtg cct gat aac ctg agt atg      679
Tyr Ile Leu Leu Pro Leu Asp Cys Gly Val Pro Asp Asn Leu Ser Met
                165                    170                    175
gct gac ccc aac att cgc ttc ctg gat aaa ctg ccc cag cag acc ggt      727
Ala Asp Pro Asn Ile Arg Phe Leu Asp Lys Leu Pro Gln Gln Thr Gly
            180                    185                    190
gac cgt gct ggc atc aag gat cgg gtt tac agc aac agc atc tat gag      775
Asp Arg Ala Gly Ile Lys Asp Arg Val Tyr Ser Asn Ser Ile Tyr Glu
        195                    200                    205
ctt ctg gag aac ggg cag cgg gcg ggc acc tgt gtc ctg gag tac gcc      823
Leu Leu Glu Asn Gly Gln Arg Ala Gly Thr Cys Val Leu Glu Tyr Ala
    210                    215                    220                    225
acc ccc ttg cag act ttg ttt gcc atg tca caa tac agt caa gct ggc      871
Thr Pro Leu Gln Thr Leu Phe Ala Met Ser Gln Tyr Ser Gln Ala Gly
                    230                    235                    240
ttt agc cgg gag gat agg ctt gag cag gcc aaa ctc ttc tgc cgg aca      919
Phe Ser Arg Glu Asp Arg Leu Glu Gln Ala Lys Leu Phe Cys Arg Thr
                245                    250                    255
ctt gag gac atc ctg gca gat gcc cct gag tct cag aac aac tgc cgc      967
Leu Glu Asp Ile Leu Ala Asp Ala Pro Glu Ser Gln Asn Asn Cys Arg
            260                    265                    270
ctc att gcc tac cag gaa cct gca gat gac agc agc ttc tcg ctg tcc     1015
Leu Ile Ala Tyr Gln Glu Pro Ala Asp Asp Ser Ser Phe Ser Leu Ser
        275                    280                    285
cag gag gtt ctc cgg cac ctg cgg cag gag gaa aag gaa gag gtt acc     1063
Gln Glu Val Leu Arg His Leu Arg Gln Glu Glu Lys Glu Glu Val Thr
    290                    295                    300                    305
gtg ggc agc ttg aag acc tca gcg gtg ccc agt acc tcc acg atg tcc     1111
Val Gly Ser Leu Lys Thr Ser Ala Val Pro Ser Thr Ser Thr Met Ser
                    310                    315                    320
caa gag cct gag ctc ctc ctc agt gga atg gga aag ccc ctc cct ctc     1159
Gln Glu Pro Glu Leu Leu Leu Ser Gly Met Gly Lys Pro Leu Pro Leu
                325                    330                    335
cgc acg gat ttc tct tgagacccag ggtcaccagg ccagagcctc cagtggtctc     1214
Arg Thr Asp Phe Ser
            340
caagcctctg gactgggggc tctcttcagt ggctgaatgt ccagcagagc tatttccttc   1274
cacagggggc cttgcaggga agggtccagg acttgacatc ttaagatgcg tcttgtcccc   1334
ttgggccagt catttcccct ctctgagcct cggtgtcttc aacctgtgaa atgggatcat   1394
aatcactgcc ttacctcccct cacggttgtt gtgaggactg agtgtgtgga agtttttcat   1454
aaactttgga tgctagtgta cttaaaaaaa aaaaaa                             1490
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<210> 91
<211> 361

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<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 26..361

<221> polyA_site
<222> 350..361

<400> 91
tcgagaagct gccccttagc caacc atg ccg tct gag ggt cgc tgc tgg gag      52
                            Met Pro Ser Glu Gly Arg Cys Trp Glu
                            1               5

acc ttg aag gcc cta cgc agt tcc gac aaa ggt cgc ctt tgc tac tac     100
Thr Leu Lys Ala Leu Arg Ser Ser Asp Lys Gly Arg Leu Cys Tyr Tyr
10                  15                  20                  25

cgc gac tgg ctg ctg cgg cgc gag gat gtt tta gaa gaa tgt atg tct     148
Arg Asp Trp Leu Leu Arg Arg Glu Asp Val Leu Glu Glu Cys Met Ser
                30                  35                  40

ctt ccc aag cta tct tct tat tct gga tgg gtg gta gag cac gtc cta     196
Leu Pro Lys Leu Ser Ser Tyr Ser Gly Trp Val Val Glu His Val Leu
            45                  50                  55

ccc cat atg cag gag aac caa cct ctg tct gag act tcg cca tcc tct     244
Pro His Met Gln Glu Asn Gln Pro Leu Ser Glu Thr Ser Pro Ser Ser
        60                  65                  70

acg tca gct tca gcc cta gat caa ccc tca ttt gtt ccc aaa tct cct     292
Thr Ser Ala Ser Ala Leu Asp Gln Pro Ser Phe Val Pro Lys Ser Pro
    75                  80                  85

gac gca agc tct gcc ttt tcc cca gcc tcc cct gca aca cca aat gga     340
Asp Ala Ser Ser Ala Phe Ser Pro Ala Ser Pro Ala Thr Pro Asn Gly
90                  95                  100                 105

acc aag ggc aaa aaa aaa aaa                                         361
Thr Lys Gly Lys Lys Lys Lys
                110


<210> 92
<211> 605
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 3..131

<221> polyA_site
<222> 591..605

<400> 92
ca tcc ctt ccc cag gct tta tgg ttc cag ttc ttc tac cac tct gga       47
   Ser Leu Pro Gln Ala Leu Trp Phe Gln Phe Phe Tyr His Ser Gly
   1               5                   10                  15

agc tcc cta gaa tct cct gga atg ctt aat gga cct ttc cag cac cga      95
Ser Ser Leu Glu Ser Pro Gly Met Leu Asn Gly Pro Phe Gln His Arg
                20                  25                  30

aat tca aga att atg act cat cgg tca gca gaa aag tgaggatacc          141
Asn Ser Arg Ile Met Thr His Arg Ser Ala Glu Lys
            35                  40

ttttcctaac ctacctgctt cccctgcagt ttcctcacaa tcttactctt tatattttag   201
catatgtagc ttctcaggat gttaattctg ttctctctgt gttggtgtct gagcacccag   261
```

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aaggtagagc caggggcact tataaaccag gagcattatt tgacaggcac ttaagaaaga     321
cactggctac gtaatcccag cactttggga ggctgaggcg gatggatcac atgaggtcag     381
gagttcgaga ccagcctggc cagcatggtg aaaccctgtc tctactaaaa atacaaaaat     441
tagctgggtg tggttgcaca cgcctgtaat cccagctacc tgggaggctg aggcaggaga     501
atcgcttgaa cttgggaggc ggaggttgca gtgagcctag attttgccat tgcactccag     561
cctgggtgac aagggcgaaa ctccatccca aaaaaaaaaa aaaa                      605
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<210> 93
<211> 591
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 33..185

<221> sig_peptide
<222> 33..80
<223> Von Heijne matrix
score 3.7
seq IALTLIPSMLSRA/AG

<221> polyA_signal
<222> 570..575

<221> polyA_site
<222> 586..591

<400> 93

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caatcttctc agcttataac cgtctttccc tt atg cta agg ata gcc ctt aca        53
                                    Met Leu Arg Ile Ala Leu Thr
                                            -15                 -10
ctc atc cca tct atg ctg tca agg gct gct ggt tgg tgc tgg tac aag       101
Leu Ile Pro Ser Met Leu Ser Arg Ala Ala Gly Trp Cys Trp Tyr Lys
                -5                  1               5
gag ccc act cag cag ttt tct tac ctt tgc ctg ccc tgc ctt tca tgg       149
Glu Pro Thr Gln Gln Phe Ser Tyr Leu Cys Leu Pro Cys Leu Ser Trp
        10                  15                  20
aat aag aaa ggc aac gtt ttg cag ctt cca aat ttc tgaagaaact            195
Asn Lys Lys Gly Asn Val Leu Gln Leu Pro Asn Phe
    25                  30                  35
aatctcagat tggcagttaa agtcaaaatg ttgccaaata tttattcctt ttgcctaagt     255
ttggctaccc ggttcaattg ctttttattt ttaatgtctt gactcttcag agttcgtacc     315
tcaaaagaac aatgagaaca tttgctttgc tttctgctga atccctaatc tcaacaatct     375
atacctggac tgtccagttc tcctcctgtg ctatcttctc ttctatccaa gtagaatgta     435
tgccaggagc tccttccctc tagcaatttc tactaaaatg tccaagtaga atgtttcctt     495
ttacaatcaa attactgtat ttattaattt gctagaatcc agtaaatcat tttggtagct     555
ctggctgtgc tatcaataaa aagatgaaag caaaaa                               591
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<210> 94
<211> 1150
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 184..915

<221> sig_peptide
<222> 184..237
<223> Von Heijne matrix
score 3.5
seq LLGLELSEAEAIG/AD

<221> polyA_signal
<222> 1119..1124

<221> polyA_site
<222> 1139..1150

<400> 94
cggatttgac gatggtgttc ggtcttgaat ggaaatgtag tcttaggcca gtcttaggtt 60
tttgaacagg atagtaggta tccggagtcg attgagggcc agagcaggca ctggggttcg 120
gatcctgggc aaagtttccc acgttgaggg tctcgaggac gcctagatct ctttcccagg 180
gcc atg gcg aac ccg aag ctg ctg gga ctg gag cta agc gag gcg gag 228
Met Ala Asn Pro Lys Leu Leu Gly Leu Glu Leu Ser Glu Ala Glu
-15 -10 -5
gcg atc ggt gct gat tcg gcg cga ttt gag gag ctg ctg ctg cag gcc 276
Ala Ile Gly Ala Asp Ser Ala Arg Phe Glu Glu Leu Leu Leu Gln Ala
1 5 10
tcg aag gag ctc cag caa gcc cag aca acc aga cca gaa tcg aca caa 324
Ser Lys Glu Leu Gln Gln Ala Gln Thr Thr Arg Pro Glu Ser Thr Gln
15 20 25
atc cag cct cag cct ggt ttc tgc ata aag acc aac tcc tcg gaa ggg 372
Ile Gln Pro Gln Pro Gly Phe Cys Ile Lys Thr Asn Ser Ser Glu Gly
30 35 40 45
aag gtt ttc atc aac atc tgc cac tcc ccc tct atc cct cct ccc gcc 420
Lys Val Phe Ile Asn Ile Cys His Ser Pro Ser Ile Pro Pro Pro Ala
50 55 60
gac gtg acc gag gag gag ctg ctt cag atg cta gag gag gac caa gct 468
Asp Val Thr Glu Glu Glu Leu Leu Gln Met Leu Glu Glu Asp Gln Ala
65 70 75
ggg ttt cgc atc ccc atg agt ctg gga gag cct cat gca gaa ctg gat 516
Gly Phe Arg Ile Pro Met Ser Leu Gly Glu Pro His Ala Glu Leu Asp
80 85 90
gca aaa ggc cag gga tgt acc gcc tac gac gta gct gtc aac agc gac 564
Ala Lys Gly Gln Gly Cys Thr Ala Tyr Asp Val Ala Val Asn Ser Asp
95 100 105
ttc tac cgg agg atg cag aac agc gat ttc ttg cgg gag ctc gtg atc 612
Phe Tyr Arg Arg Met Gln Asn Ser Asp Phe Leu Arg Glu Leu Val Ile
110 115 120 125
acc atc gcc agg gag ggc ctt gag gac ata tac aac ttg cag ctg aat 660
Thr Ile Ala Arg Glu Gly Leu Glu Asp Ile Tyr Asn Leu Gln Leu Asn
130 135 140
ccg gaa tgg cgc atg atg aag aac cgg cca ttc atg ggc tcc atc tcg 708
Pro Glu Trp Arg Met Met Lys Asn Arg Pro Phe Met Gly Ser Ile Ser
145 150 155
cag cag aac atc cgc tcg gag cag cgt cct cgg atc cag gag ctg ggg 756
Gln Gln Asn Ile Arg Ser Glu Gln Arg Pro Arg Ile Gln Glu Leu Gly
160 165 170
gac ctg tac acg ccc gcc ccc ggg aga gct gag tca ggg cct gaa aag 804
Asp Leu Tyr Thr Pro Ala Pro Gly Arg Ala Glu Ser Gly Pro Glu Lys
175 180 185
cct cac ctg aac ctg tgg ctg gaa gcc ccc gac ctc ctc ttg gcc gaa 852
Pro His Leu Asn Leu Trp Leu Glu Ala Pro Asp Leu Leu Leu Ala Glu
190 195 200 205
gtt gac ctc ccc aaa ctg gat gga gcc ctg ggg ctg tcg ctg gag atc 900
Val Asp Leu Pro Lys Leu Asp Gly Ala Leu Gly Leu Ser Leu Glu Ile
210 215 220
ggg aga acc gcc tgg tgatgggggg cccccagcag ctgtatcatc tagacgctta 955

Gly Arg Thr Ala Trp
225
tatcccgccg cagatcaact ctcatgagag caaggcagcc ttccaccgga agagaaagca 1015
attaatggtg gccatgccgc ttctgccggt gccttcttga tcagggtgtc tccttgtgct 1075
tctgagatgt ggagaagagg ctgctggctt ccctaaagt tgaaataaaa gatttttgcc 1135
tttaaaaaaa aaaaa 1150

<210> 95
<211> 1513
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 58..1116

<221> sig_peptide
<222> 58..159
<223> Von Heijne matrix
score 4
seq IAVLYLHLYDVFG/DP

<221> polyA_signal
<222> 1486..1491

<221> polyA_site
<222> 1504..1513

<400> 95
ctgactcctg agttctcaca acgcttgacc aataagattc gggagcttct tcagcaa 57
atg gag aga ggc ctg aaa tca gca gac cct cgg gat ggc acc ggt tac 105
Met Glu Arg Gly Leu Lys Ser Ala Asp Pro Arg Asp Gly Thr Gly Tyr
-30 -25 -20
act ggc tgg gca ggt att gct gtg ctt tac tta cat ctt tat gat gta 153
Thr Gly Trp Ala Gly Ile Ala Val Leu Tyr Leu His Leu Tyr Asp Val
-15 -10 -5
ttt ggg gac cct gcc tac cta cag tta gca cat ggc tat gta aag caa 201
Phe Gly Asp Pro Ala Tyr Leu Gln Leu Ala His Gly Tyr Val Lys Gln
1 5 10
agt ctg aac tgc tta acc aag cgc tcc atc acc ttc ctt tgt ggg gat 249
Ser Leu Asn Cys Leu Thr Lys Arg Ser Ile Thr Phe Leu Cys Gly Asp
15 20 25 30
gca ggc ccc ctg gca gtg gcc gct gtg cta tat cat aag atg aac aat 297
Ala Gly Pro Leu Ala Val Ala Ala Val Leu Tyr His Lys Met Asn Asn
35 40 45
gag aag cag gca gaa gat tgc atc aca cgg cta att cac cta aat aag 345
Glu Lys Gln Ala Glu Asp Cys Ile Thr Arg Leu Ile His Leu Asn Lys
50 55 60
att gat cct cat gct cca aat gaa atg ctc tat ggg cga ata ggc tac 393
Ile Asp Pro His Ala Pro Asn Glu Met Leu Tyr Gly Arg Ile Gly Tyr
65 70 75
atc tat gct ctt ctt ttt gtc aat aag aac ttt gga gtg gaa aag act 441
Ile Tyr Ala Leu Leu Phe Val Asn Lys Asn Phe Gly Val Glu Lys Thr
80 85 90
cct caa agc cat att cag cag att tgt gaa aca att tta acc tct gga 489
Pro Gln Ser His Ile Gln Gln Ile Cys Glu Thr Ile Leu Thr Ser Gly
95 100 105 110
gaa aac cta gct agg aag aga aac ttc acg gca aag tct cca ctg atg 537
Glu Asn Leu Ala Arg Lys Arg Asn Phe Thr Ala Lys Ser Pro Leu Met
115 120 125

```
tat gaa tgg tac cag gaa tat tat gta ggg gct gct cat ggc ctg gct      585
Tyr Glu Trp Tyr Gln Glu Tyr Tyr Val Gly Ala Ala His Gly Leu Ala
            130                 135                 140
gga att tat tac tac ctg atg cag ccc agc ctt caa gtg agc caa ggg      633
Gly Ile Tyr Tyr Tyr Leu Met Gln Pro Ser Leu Gln Val Ser Gln Gly
        145                 150                 155
aag tta cat agt ttg gtc aag ccc agt gta gac tac gtc tgc cag ctg      681
Lys Leu His Ser Leu Val Lys Pro Ser Val Asp Tyr Val Cys Gln Leu
    160                 165                 170
aaa ttc cct tct ggc aat tac cct cca tgt ata ggt gat aat cga gat      729
Lys Phe Pro Ser Gly Asn Tyr Pro Pro Cys Ile Gly Asp Asn Arg Asp
175                 180                 185                 190
ctg ctt gtc cat tgg tgc cat ggc gcc cct ggg gta atc tac atg ctc      777
Leu Leu Val His Trp Cys His Gly Ala Pro Gly Val Ile Tyr Met Leu
                195                 200                 205
atc cag gcc tat aag gta ttc aga gag gaa aag tat ctc tgt gat gcc      825
Ile Gln Ala Tyr Lys Val Phe Arg Glu Glu Lys Tyr Leu Cys Asp Ala
            210                 215                 220
tat cag tgt gct gat gtg atc tgg caa tat ggg ttg ctg aag aag gga      873
Tyr Gln Cys Ala Asp Val Ile Trp Gln Tyr Gly Leu Leu Lys Lys Gly
        225                 230                 235
tat ggg ctg tgc cac ggt tct gca ggg aat gcc tat gcc ttc ctg aca      921
Tyr Gly Leu Cys His Gly Ser Ala Gly Asn Ala Tyr Ala Phe Leu Thr
    240                 245                 250
ctc tac aac ctc aca cag gac atg aag tac ctg tat agg gcc tgt aag      969
Leu Tyr Asn Leu Thr Gln Asp Met Lys Tyr Leu Tyr Arg Ala Cys Lys
255                 260                 265                 270
ttt gct gaa tgg tgc tta gag tat gga gaa cat gga tgc aga aca cca     1017
Phe Ala Glu Trp Cys Leu Glu Tyr Gly Glu His Gly Cys Arg Thr Pro
                275                 280                 285
gac acc cct ttc tct ctc ttt gaa gga atg gct ggg aca ata tat ttc     1065
Asp Thr Pro Phe Ser Leu Phe Glu Gly Met Ala Gly Thr Ile Tyr Phe
            290                 295                 300
ctg gct gac ctg cta gtc ccc aca aaa gcc agg ttc cct gca ttt gaa     1113
Leu Ala Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu
        305                 310                 315
ctc tgaaaggata gcatgccacc tgcaactcac tgcatgaccc tttctgtata          1166
Leu
ttcaaaccca agctaagtgc ttccgttgct ttccaaggaa acaaagagtc aaactgtgga   1226
cttgattttg ttagcttttt tcagaattta tctttcattc agttcccttc cattatcatt   1286
tacttttact tagaagtatc caaggaagtc ttttaacttt aatttccatt tcttcctaaa   1346
gggagagtga gtgatatgta cagtgttttg agattgtata catatattcc agaacttgga   1406
ggaaatctta tttaagttta tgaatataac catctgttac tgttctaaaa atgtttaaaa   1466
gaaactcaat acagataaag ataaatatgt gactattaaa aaaaaaa                 1513
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<210> 96
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 327..416

<221> polyA_site
<222> 404..417

<400> 96

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tgttttgagg tgttggcatt cttcgctgat ttggctgttc ccaatgttta cattatttaa     60
tcttgcaaaa atggttctgt gcacttggat gtgaaatgct gtccagtttt attttttta     120
```

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tgttgttatc cttggatgta caaaaaattc agaaaatgat ctctgtagat attctgtttt    180
atttggtca tctttagaag ttatcaggaa tgtgtttaaa acaagaagag aacttttcta    240
aggaatgata catagaaaag attttatttt aaaatgagtt gtaaagcttg tgtttctttg    300
ttgctgcaag ctatctgccc aagtta atg caa atg gac aca ttt ttt atg tca    353
                             Met Gln Met Asp Thr Phe Phe Met Ser
                             1               5
gaa aaa cac aca cac aca cac aca cat ata cac aca cac aca cga aaa     401
Glu Lys His Thr His Thr His Thr His Ile His Thr His Thr Arg Lys
10                  15                  20                  25
aca aaa aaa aaa aaa a                                              417
Thr Lys Lys Lys Lys
            30
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<210> 97
<211> 603
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 63..398

<221> sig_peptide
<222> 63..206
<223> Von Heijne matrix
score 4.9
seq PSLAAGLLFGSLA/GL

<400> 97

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ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa     60
aa atg cag gac act ggc tca gta gtg cct ttg cat tgg ttt ggc ttt      107
   Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe
               -45                 -40                 -35
ggc tac gca gca ctg gtt gct tct ggt ggg atc att ggc tat gta aaa    155
Gly Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys
            -30                 -25                 -20
gca ggc agc gtg ccg tcc ctg gct gca ggg ctg ctc ttt ggc agt cta    203
Ala Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu
        -15                 -10                 -5
gcc ggc ctg ggt gct tac cag ctg tct cag gat cca agg aac gtt tgg    251
Ala Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp
    1               5                   10                  15
gtt ttc cta gct aca tct ggt acc ttg gct ggc att atg gga atg agg    299
Val Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg
                20                  25                  30
ttc tac cac tct gga aaa ttc atg cct gca ggt tta att gca ggt gcc    347
Phe Tyr His Ser Gly Lys Phe Met Pro Ala Gly Leu Ile Ala Gly Ala
            35                  40                  45
agt ttg ctg atg gtc gcc aaa gtt gga gtt agt atg ttc aac aga ccc    395
Ser Leu Leu Met Val Ala Lys Val Gly Val Ser Met Phe Asn Arg Pro
        50                  55                  60
cat tagcagaagt catgttccag cttagactga tgaagaatta aaaatctgca         448
His
tcttccacta ttttcaatat attaagagaa ataagtgcag catttttgca tctgacattt   508
tacctaaaaa aaaagacacc aaacttggca gagaggtgga aaatcagtca tgattacaaa   568
cctacagagg tggcgagtat gtaacacaag agctt                              603
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<210> 98

<211> 522
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..163

<221> polyA_signal
<222> 488..493

<221> polyA_site
<222> 511..522

<400> 98
c gag att gcg ggc tat ggc gcc gaa ggt ttt tcg tca gta ctg gga tat 49
Glu Ile Ala Gly Tyr Gly Ala Glu Gly Phe Ser Ser Val Leu Gly Tyr
1 5 10 15
ccc cga tgg cac cga ttg cca ccg caa agc cta cag cac cac cag tat 97
Pro Arg Trp His Arg Leu Pro Pro Gln Ser Leu Gln His His Gln Tyr
20 25 30
tgc cag cgt cgc tgg cct gac cgc cgc tgc cta cag agt cac act caa 145
Cys Gln Arg Arg Trp Pro Asp Arg Arg Cys Leu Gln Ser His Thr Gln
35 40 45
tcc tcc ggg cac ctt cct nntgaaggag tggctaaggt tggacaatac 193
Ser Ser Gly His Leu Pro
50
acgttcactg cagctgctgt cggggccgtg tttggcctca ccacctgcat cagcgcccat 253
gtccgcgaga agcccgacga ccccctgaac tacttccccg gtggctgcgc cnggaggcct 313
gactctggga gcacgcacgc acaactacgg gattggcgcc gccgcctgcg tgtactttgg 373
catagcggcc tccctggtca agatgggccg gctggagggc tgggaggtgt ttgcaaaacc 433
caaggtgtga gccctgtgcc tgccgggacc tccagcctgc agaatgcgtc cagaaataaa 493
ttctgtgtct gtgtgtgaaa aaaaaaaa 522

<210> 99
<211> 956
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 13..465

<221> sig_peptide
<222> 13..75
<223> Von Heijne matrix
score 3.9
seq PVAVTAAVAPVLS/IN

<400> 99
ngagtcggga aa atg gct gcg agt acn tcn atg gnc ccg gtg gct gtg acg 51
Met Ala Ala Ser Thr Ser Met Xaa Pro Val Ala Val Thr
-20 -15 -10
gcg gca gtg gcg cct gtc ctg tcc ata aac agc gat ttc tca gat ttg 99
Ala Ala Val Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu
-5 1 5
cgg gaa att aaa aag caa ctg ctg ctt att gcg ggc ctt acc cgg gag 147
Arg Glu Ile Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu
10 15 20
cgg ggc cta cta cac agt agc aaa tgg tcg gcg gag ttg gct ttc tct 195

```
Arg Gly Leu Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser
25                  30                  35                  40
ctc cct gca ttg cct cnt ggc cag ctg caa ccg cct ccg cct att aca        243
Leu Pro Ala Leu Pro Xaa Gly Gln Leu Gln Pro Pro Pro Pro Ile Thr
                45                  50                  55
gag gaa gat gcc cag gat atg gat gcc tat acc ctg gcc aag gcc tac        291
Glu Glu Asp Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr
            60                  65                  70
ttt gac gtt aaa gag tat gat cgg gca gca cat ttc ctg cat ggc tgc        339
Phe Asp Val Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys
        75                  80                  85
aat agc aag aaa gcc tat ttt ctg tat atg tat tcc aga tat ctg gtg        387
Asn Ser Lys Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val
    90                  95                  100
agg gcc att tta aaa tgt cat tct gcc ttt agt gaa aca tcc ata ttt        435
Arg Ala Ile Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe
105                 110                 115                 120
aga acc aat gga aaa gtt aaa tct ttt aaa tagcttagca gtgggccact          485
Arg Thr Asn Gly Lys Val Lys Ser Phe Lys
                125                 130
gaatgaatgt actttataca tagcaataat aaaaaaaaga tatcataaat aaagttaaaa      545
aggatggtag agaagaaaat attcttagga atgactaaca ggataagtaa caacctgatt      605
atttatttac tttaggttat ataaggttct tcatgcctgt gaattaatat tattgtgtaa      665
gaattaagtt aaaaagcctg ggctgacttt taaatttata aattcattta tcatgtttat      725
agtatattta ttgtttttct ttcatggcta ttaaaaagta tgactgtaaa ggacaatgca      785
agnaaaccaa cttaatactg tattgaataa taagtacaat ttattatttt actttgaaac      845
attatgaatt tactttccta ctttttctta gttgttatct atataaattg attaaaaaaa      905
cattttatgt acntnncatt tcctagtaca ggttgagtat cccttatttg a               956


<210> 100
<211> 1041
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 20..703

<221> sig_peptide
<222> 20..94
<223> Von Heijne matrix
      score 3.9
      seq ATVGLLMLGVTLP/NS

<221> polyA_signal
<222> 1000..1005

<221> polyA_site
<222> 1023..1041

<400> 100
cagggtcctg catcctacc atg tcg atg gct gtg gaa acc ttt ggc ttc ttc        52
                     Met Ser Met Ala Val Glu Thr Phe Gly Phe Phe
                     -25                 -20                 -15
atg gca act gtg ggg ctg ctg atg ctg ggg gtg act ctg cca aac agc        100
Met Ala Thr Val Gly Leu Leu Met Leu Gly Val Thr Leu Pro Asn Ser
                -10                 -5                  1
tac tgg cga gtg tcc act gtg cac ggg aac gtc atc acc acc aac acc        148
Tyr Trp Arg Val Ser Thr Val His Gly Asn Val Ile Thr Thr Asn Thr
        5                   10                  15
```

atc ttc gag aac ctc tgg ttt agc tgt gcc acc gac tcc ctg ggc gtc 196
Ile Phe Glu Asn Leu Trp Phe Ser Cys Ala Thr Asp Ser Leu Gly Val
20 25 30
tac aac tgc tgg gag ttc ccg tcc atg ctg gcc ctc tct ggg tat att 244
Tyr Asn Cys Trp Glu Phe Pro Ser Met Leu Ala Leu Ser Gly Tyr Ile
35 40 45 50
cag gcc tgc cgg gca ctc atg atc acc gcc atc ctc ctg ggc ttc ctc 292
Gln Ala Cys Arg Ala Leu Met Ile Thr Ala Ile Leu Leu Gly Phe Leu
55 60 65
ggc ctc ttg cta ggc ata gcg ggc ctg cgc tgc acc aac att ggg ggc 340
Gly Leu Leu Leu Gly Ile Ala Gly Leu Arg Cys Thr Asn Ile Gly Gly
70 75 80
ctg gag ctc tcc agg aaa gcc aag ctg gcg gcc acc gca ggg gcc ccc 388
Leu Glu Leu Ser Arg Lys Ala Lys Leu Ala Ala Thr Ala Gly Ala Pro
85 90 95
cac att ctg gcc ggt atc tgc ggg atg gtg gcc atc tcc tgg tac gcc 436
His Ile Leu Ala Gly Ile Cys Gly Met Val Ala Ile Ser Trp Tyr Ala
100 105 110
ttc aac atc acc cgg gac ttc ttc gac ccc ttg tac ccc gga acc aag 484
Phe Asn Ile Thr Arg Asp Phe Phe Asp Pro Leu Tyr Pro Gly Thr Lys
115 120 125 130
tac gag ctg ggc ccc gcc ctc tac ctg ggg tgg agc gcc tca ctg atc 532
Tyr Glu Leu Gly Pro Ala Leu Tyr Leu Gly Trp Ser Ala Ser Leu Ile
135 140 145
tcc atc ctg ggt ggc ctc tgc ctc tgc tcc gcc tgc tgc tgc ggc tct 580
Ser Ile Leu Gly Gly Leu Cys Leu Cys Ser Ala Cys Cys Cys Gly Ser
150 155 160
gac gag gac cca gcc gcc agc gcc cgg cgg ccc tac cag gct cca gtg 628
Asp Glu Asp Pro Ala Ala Ser Ala Arg Arg Pro Tyr Gln Ala Pro Val
165 170 175
tcc gtg atg ccc gtc gcc acc tcg gac caa gaa ggc gac agc agc ttt 676
Ser Val Met Pro Val Ala Thr Ser Asp Gln Glu Gly Asp Ser Ser Phe
180 185 190
ggc aaa tac ggc aga aac gcc tac gtg tagcagctct ggcccgtggg 723
Gly Lys Tyr Gly Arg Asn Ala Tyr Val
195 200
ccccgctgtc ttcccactgc cccaaggaga ggggacctgg ccggggccca ttcccctata 783
gtaacctcag ggccggccca cgcccсgctc ccgtagcccc gccccggcca cggccccgtg 843
tcttgcactc tcatggcccc tccaggccaa gaactgctct tgggaagtcg catatctccc 903
ctctgaggct ggatccctca tcttctgacc ctgggttctg ggctgtgaag gggacggtgt 963
ccccgcacgt ttgtattgtg tataaataca ttcattaata aatgcatatt gtgaccgtta 1023
aaaaaaaaaa aaaaaaaa 1041

<210> 101
<211> 558
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 103..294

<221> sig_peptide
<222> 103..243
<223> Von Heijne matrix
score 5.9
seq TWLGLLSFQNLHC/FP

<400> 101
ttccccatggt ttagaagcat aacctgtaat gtaatgcaag tcccctaact ccctggttgc 60

```
taacattaac ttccttaagt aataatcaat gaaagaaatt ct atg cat ggt ttt       114
                                               Met His Gly Phe
                                                       -45
gaa ata ata tcc ttg aaa gag gaa tca cca tta gga aag gtg agt cag      162
Glu Ile Ile Ser Leu Lys Glu Glu Ser Pro Leu Gly Lys Val Ser Gln
            -40                 -35                 -30
ggt cct ttg ttt aat gtg act agt ggc tca tca tca cca gtg acc tgg      210
Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Ser Pro Val Thr Trp
        -25                 -20                 -15
ttg ggc cta ctc tcc ttc cag aac ctg cat tgc ttc cca gac ctc ccc      258
Leu Gly Leu Leu Ser Phe Gln Asn Leu His Cys Phe Pro Asp Leu Pro
    -10                 -5                  1               5
act gag atg cct cta aga gcc aaa gga gtc aac act tgagcctagg           304
Thr Glu Met Pro Leu Arg Ala Lys Gly Val Asn Thr
                10                  15
gtgggctaca acaaaagatt ctaatttacc ttgcttcatc taggtccagg ccccaagtag    364
cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataagc taaaaacatt    424
tatttttgtt gaatcgaaac aattccatgt agcaatcttt tttctgttca cggtgtttgt    484
gatagaacct taaattccgc aagcatcagt tttttgaaaa aatgggaatt gaccggatag    544
taacaggcaa agtt                                                      558
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<210> 102
<211> 730
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 81..518

<221> sig_peptide
<222> 81..173
<223> Von Heijne matrix
score 3.9
seq ILFHGVFYAGGFA/IV

<400> 102

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ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg     60
attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg    113
                      Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg
                              -30                 -25
tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc      161
Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala
-20                 -15                 -10                 -5
ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg      209
Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg
                1               5                   10
gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag      257
Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu
        15                  20                  25
gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc      305
Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu
    30                  35                  40
atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att      353
Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile
45                  50                  55                  60
cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc      401
Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser
                65                  70                  75
aga ggt ggc ccc ttt cag agg tgg cac ctt gac gag gtc ttt tta gag      449
```

Arg Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu
80 85 90
ctc aag gat ggt cag cag att cct gtg ttc aag ctc agt ggg gaa aac 497
Leu Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn
95 100 105
ggt gat gaa gtg aaa aag gag tagagacgac ccagaagacc cagcttgctt 548
Gly Asp Glu Val Lys Lys Glu
110 115
ctagtccatc cttccctcat ctctaccata tggccactgg ggtggtggcc catctcagtg 608
acagacactc ctgcaaccca gttttccagc caccagtggg atgatggtat gtgccagcac 668
atggtaattt tggtgtaatt ctaacttggg cacaacgaat gctatttgtc atttttaaac 728
tg 730

<210> 103
<211> 1098
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 66..326

<221> polyA_signal
<222> 1066..1071

<221> polyA_site
<222> 1087..1098

<400> 103
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc 60
ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc 110
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser
1 5 10 15
ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac 158
Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His
20 25 30
ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc 206
Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro
35 40 45
gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag 254
Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln
50 55 60
tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag 302
Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu
65 70 75
ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca 356
Leu Glu Val Asp Asp Trp Glu Phe
80 85
gccagggatg cagaggccac ccagaggccc ttcctgaggg ccggccacat tcccgccctc 416
ctgggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg ctgattggga 476
aagaaaatcc tggagagata cttcactgct ccaaggcttt tgagacacaa gggaatctca 536
acaaccaggg atcaggaggg tccaaagccg acattcccag tcctgtgagc tcaggtgacc 596
tcctccgcag aagagagatg ctgctctggc cctgggagct gaattccaag cccagggttt 656
ggctccttaa acccgaggac cgccacctct tcccagtgct tgcgaccagc ctcattctac 716
ttaactttgc tctcagatgc ctcagatgct ataggtcagt gaaagggcga gtagtaagct 776
gcctgcctcc cttccctcag acctctccct cataattcca gagaagggca tttctgtctt 836
tttaagcaca gactaaggct ggaacagtcc atccttatcc ctcttctggc ttgggccctg 896
acacctaagt ctttcccacg gtttatgtgt gtgcctcatt cctttcccac caagaatcca 956
tcttagcgcc tcctgccagc tgccctggtg ctttctccaa gggccatcag tgtcttgcct 1016
agcttgaggg cttaagtcct tatgctgtgt tagtttcgtt gtcagaacaa attaaaattt 1076

tcagagacgc aaaaaaaaaa aa 1098

<210> 104
<211> 346
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 170..289

<221> sig_peptide
<222> 170..250
<223> Von Heijne matrix
score 3.6
seq LTLLLITPSPSPL/LF

<400> 104
ccatttgagc cccaccacgg aggttatgtg gtcccaaaag gaatgatggc caagcaatta 60
atttttcctc ctagttctta gcttgcttct gcattgattg gctttacaca actggcattt 120
agtctgcatt acacaaatag acactaattt atttggaaca agcagcaaa atg aga act 178
Met Arg Thr
-25
tta ttt ggt gca gtc agg gct cca ttt agt tcc ctc act ctg ctt cta 226
Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr Leu Leu Leu
-20 -15 -10
atc acc cct tct ccc agc cct ctt cta ttt gat aga ggt ctg tcc ctc 274
Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly Leu Ser Leu
-5 1 5
aga tca gca atg tct tagcccctct cctctcttcc attccttcct gttggtactc 329
Arg Ser Ala Met Ser
10
atttcttcta actttta 346

<210> 105
<211> 685
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 36..497

<221> polyA_signal
<222> 650..655

<221> polyA_site
<222> 663..685

<400> 105
aagttctgcg ctggtcggcg gagtagcaag tggcc atg ggg agc ctc agc ggt 53
Met Gly Ser Leu Ser Gly
1 5
ctg cgc ctg gca gca gga agc tgt ttt agg tta tgt gaa aga gat gtt 101
Leu Arg Leu Ala Ala Gly Ser Cys Phe Arg Leu Cys Glu Arg Asp Val
10 15 20
tcc tca tct cta agg ctt acc aga agc tct gat ttg aag aga ata aat 149
Ser Ser Ser Leu Arg Leu Thr Arg Ser Ser Asp Leu Lys Arg Ile Asn

25 30 35
gga ttt tgc aca aaa cca cag gaa agt ccc gga gct cca tcc cgc act 197
Gly Phe Cys Thr Lys Pro Gln Glu Ser Pro Gly Ala Pro Ser Arg Thr
40 45 50
tac aac aga gtg cct tta cac aaa cct acg gat tgg cag aaa aag atc 245
Tyr Asn Arg Val Pro Leu His Lys Pro Thr Asp Trp Gln Lys Lys Ile
55 60 65 70
ctc ata tgg tca ggt cgc ttc aaa aag gaa gat gaa atc cca gag act 293
Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu Asp Glu Ile Pro Glu Thr
75 80 85
gtc tcg ttg gag atg ctt gat gct gca aag aac aag atg cga gtg aag 341
Val Ser Leu Glu Met Leu Asp Ala Ala Lys Asn Lys Met Arg Val Lys
90 95 100
agc agc tat cta atg att gcc ctg acg gtg gta gga tgc atc ttc atg 389
Ser Ser Tyr Leu Met Ile Ala Leu Thr Val Val Gly Cys Ile Phe Met
105 110 115
gtt att gag ggc aag aag gct gcc caa aga cac gag act tta aca agc 437
Val Ile Glu Gly Lys Lys Ala Ala Gln Arg His Glu Thr Leu Thr Ser
120 125 130
ttg aac tta gaa aag aaa gct cgt ctg aaa gag gaa gca gct atg aag 485
Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys Glu Glu Ala Ala Met Lys
135 140 145 150
gcc aaa aca gag tagcagaggt atccgtgttg gctggatttt gaaaatccag 537
Ala Lys Thr Glu
gaattatgtt ataacgtgcc tgtattaaaa aggatgtggt atgaggatcc atttcataaa 597
gtatgatttg cccaaacctg taccatttcc gtatttctgc cgtagaagta gaaataaatt 657
ttcttaaaaa aaaaaaaaaa aaaaaaaa 685

<210> 106
<211> 554
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 18..320

<221> polyA_signal
<222> 539..544

<221> polyA_site
<222> 542..554

<400> 106
aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt 50
Met Val Cys Glu Lys Cys Glu Lys Lys Leu Gly
1 5 10
act gtt atc act cca gat aca tgg aaa gat ggt gct agg aat acc aca 98
Thr Val Ile Thr Pro Asp Thr Trp Lys Asp Gly Ala Arg Asn Thr Thr
15 20 25
gaa agt ggt gga aga aag ctg aat aaa aat aaa gct ttg act tca aaa 146
Glu Ser Gly Gly Arg Lys Leu Asn Lys Asn Lys Ala Leu Thr Ser Lys
30 35 40
aaa gca aga ttt gat cca tat gga aag aat aag ttc tcc act tgt aga 194
Lys Ala Arg Phe Asp Pro Tyr Gly Lys Asn Lys Phe Ser Thr Cys Arg
45 50 55
att tgt aaa agt tct gtg cac caa cca ggt tct cat tac tgc cag ggc 242
Ile Cys Lys Ser Ser Val His Gln Pro Gly Ser His Tyr Cys Gln Gly
60 65 70 75
tgt gcc tac aaa aaa ggc atc tgt gcg atg tgt ggn aaa aaa gtt ttg 290

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Cys Ala Tyr Lys Lys Gly Ile Cys Ala Met Cys Gly Lys Lys Val Leu
                80                  85                  90
gat acc aaa aac tac aag caa aca tct gtc tagatgtatt gatggaattt       340
Asp Thr Lys Asn Tyr Lys Gln Thr Ser Val
            95                  100
ctggctttct aaatgatttt actttctgcc ttgaattttc aaggcataga tgtcaactta   400
cagaataaca tgttttaaga taattaagtt taaaccagag aatttgattg ttactcattt   460
tgctctcatg ttctaaacag caacagtgta actagtcttt tgttgtaaat ggttattttc   520
cttataagaa ttttaagaac taaaaaaaaa aaaa                               554
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<210> 107
<211> 1678
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 71..1438

<221> sig_peptide
<222> 71..136
<223> Von Heijne matrix
      score 3.5
      seq AAPVAAGLGPVIS/RP

<221> polyA_signal
<222> 1644..1649

<221> polyA_site
<222> 1665..1678

<400> 107
ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct    60
cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta      109
           Met Phe Glu Glu Pro Glu Trp Ala Glu Ala Ala Pro Val
                   -20                 -15                 -10
gcc gcg ggc ctt ggg ccc gta atc tca cga cct ccg cct gcg gcc tcc     157
Ala Ala Gly Leu Gly Pro Val Ile Ser Arg Pro Pro Pro Ala Ala Ser
                -5                  1                   5
tcg caa aac aag ggc tcc aag cgc cgc cag ctc ttg gcc aca tta cgg     205
Ser Gln Asn Lys Gly Ser Lys Arg Arg Gln Leu Leu Ala Thr Leu Arg
        10                  15                  20
gcc cta gag gca gca tct ctt tcc cag cat ccc ccc agc cta tgt ata     253
Ala Leu Glu Ala Ala Ser Leu Ser Gln His Pro Pro Ser Leu Cys Ile
    25                  30                  35
agt gac tct gag gag gag gag gag gaa agg aag aag aaa tgc ccc aaa     301
Ser Asp Ser Glu Glu Glu Glu Glu Glu Arg Lys Lys Lys Cys Pro Lys
40                  45                  50                  55
aag gca tca ttt gcc agt gcc tct gct gaa gta ggg aag aaa ggg aag     349
Lys Ala Ser Phe Ala Ser Ala Ser Ala Glu Val Gly Lys Lys Gly Lys
                60                  65                  70
aag aaa tgt caa aaa cag ggc cca cct tgc agt gac tct gag gaa gaa     397
Lys Lys Cys Gln Lys Gln Gly Pro Pro Cys Ser Asp Ser Glu Glu Glu
            75                  80                  85
gta gaa agg aag aag aaa tgc cac aaa cag gct ctt gtt ggc agt gac     445
Val Glu Arg Lys Lys Lys Cys His Lys Gln Ala Leu Val Gly Ser Asp
        90                  95                  100
tct gct gaa gat gag aaa aga aag agg aaa tgc cag aaa cat gcc cct     493
Ser Ala Glu Asp Glu Lys Arg Lys Arg Lys Cys Gln Lys His Ala Pro
    105                 110                 115
```

```
ata aat tca gcc cag cac ctg gac aat gtt gac caa aca ggt ccc aaa      541
Ile Asn Ser Ala Gln His Leu Asp Asn Val Asp Gln Thr Gly Pro Lys
120                 125                 130                 135
gcc tgg aag ggt agt act aca aat gat cca cca aag caa agc cct ggg      589
Ala Trp Lys Gly Ser Thr Thr Asn Asp Pro Pro Lys Gln Ser Pro Gly
            140                 145                 150
tcc act tcc cct aaa ccc cct cat aca tta agc cgc aag cag tgg cgg      637
Ser Thr Ser Pro Lys Pro Pro His Thr Leu Ser Arg Lys Gln Trp Arg
        155                 160                 165
aac cgg caa aag aat aag aga aga tgt aag aac aag ttt cag cca cct      685
Asn Arg Gln Lys Asn Lys Arg Arg Cys Lys Asn Lys Phe Gln Pro Pro
    170                 175                 180
cag gtg cca gac cag gcc cca gct gag gcc ccc aca gag aag aca gag      733
Gln Val Pro Asp Gln Ala Pro Ala Glu Ala Pro Thr Glu Lys Thr Glu
185                 190                 195
gtg tct cct gtt ccc agg aca gac agc cat ggg gct cgg gca ggg gct      781
Val Ser Pro Val Pro Arg Thr Asp Ser His Gly Ala Arg Ala Gly Ala
200                 205                 210                 215
ttg cga gcc cgc atg gca cag cgg ctg gat ggg gcc cga ttt cgc tac      829
Leu Arg Ala Arg Met Ala Gln Arg Leu Asp Gly Ala Arg Phe Arg Tyr
            220                 225                 230
ctc aat gaa cag ttg tac tca ggg ccc agc agt gct gca cag cgt ctc      877
Leu Asn Glu Gln Leu Tyr Ser Gly Pro Ser Ser Ala Ala Gln Arg Leu
        235                 240                 245
ttc cag gaa gac cct gag gct ttt ctt ctc tac cac cgc ggc ttc cag      925
Phe Gln Glu Asp Pro Glu Ala Phe Leu Leu Tyr His Arg Gly Phe Gln
    250                 255                 260
agc caa gtg aag aag tgg cca ctg cag cca gtg gac cgc atc gcc agg      973
Ser Gln Val Lys Lys Trp Pro Leu Gln Pro Val Asp Arg Ile Ala Arg
265                 270                 275
gat ctt cgc cag cgg cct gca tcc cta gtg gtg gct gac ttc ggc tgt     1021
Asp Leu Arg Gln Arg Pro Ala Ser Leu Val Val Ala Asp Phe Gly Cys
280                 285                 290                 295
ggg gat tgc cgc ttg gct tca agt atc cgg aac cct gtg cat tgc ttt     1069
Gly Asp Cys Arg Leu Ala Ser Ser Ile Arg Asn Pro Val His Cys Phe
            300                 305                 310
gac ttg gct tct ctg gac cct agg gtc act gtg tgt gac atg gcc cag     1117
Asp Leu Ala Ser Leu Asp Pro Arg Val Thr Val Cys Asp Met Ala Gln
        315                 320                 325
gtt cct ttg gag gat gag tct gtg gat gtg gct gtg ttt tgc ctt tca     1165
Val Pro Leu Glu Asp Glu Ser Val Asp Val Ala Val Phe Cys Leu Ser
    330                 335                 340
ctg atg gga acc aac atc agg gac ttc cta gag gag gca aat aga gta     1213
Leu Met Gly Thr Asn Ile Arg Asp Phe Leu Glu Glu Ala Asn Arg Val
345                 350                 355
ctg aag cca ggg ggt ctc ctg aaa gtg gct gag gtc agc agc cgc ttt     1261
Leu Lys Pro Gly Gly Leu Leu Lys Val Ala Glu Val Ser Ser Arg Phe
360                 365                 370                 375
gag gat gtt cga acc ttt ctg cgg gct gtg acc aag cta ggc ttc aag     1309
Glu Asp Val Arg Thr Phe Leu Arg Ala Val Thr Lys Leu Gly Phe Lys
            380                 385                 390
att gtc tcc aag gac ctg acc aac agc cat ttc ttc ttg ttt gat ttc     1357
Ile Val Ser Lys Asp Leu Thr Asn Ser His Phe Phe Leu Phe Asp Phe
        395                 400                 405
caa aag act ggg ccc cct ctg gta ggg ccc aag gct cag ctt tca ggc     1405
Gln Lys Thr Gly Pro Pro Leu Val Gly Pro Lys Ala Gln Leu Ser Gly
    410                 415                 420
ctg cag ctt cag cca tgt ctc tac aag cgc agg tgacctctgg atcttccttg   1458
Leu Gln Leu Gln Pro Cys Leu Tyr Lys Arg Arg
425                 430
agaggggagg cagatctcaa actccaggct cagaactgtg aagactgttt ccggcctggc   1518
tgtgagccaa gacctggttc ctggtggacc ctgaggacaa agtgtgataa aacctctggc   1578
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tcagacttgc tctactgaag gcttcttggt tataagatgc ataaagtcac tggggctagc 1638
taaacaataa agagtttatt gtgaggaaaa aaaaaaaaaa 1678

<210> 108
<211> 494
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 25..318

<221> sig_peptide
<222> 25..75
<223> Von Heijne matrix
score 7.4
seq FFLLLQFFLRIDG/VL

<221> polyA_signal
<222> 452..457

<221> polyA_site
<222> 482..494

<400> 108
aggctgagtg tgaagattag agta atg cct tct agc ttt ttc ctg ctg ttg 51
Met Pro Ser Ser Phe Phe Leu Leu Leu
-15 -10
cag ttt ttc ttg aga att gat ggg gtg ctt atc aga atg aat gac acg 99
Gln Phe Phe Leu Arg Ile Asp Gly Val Leu Ile Arg Met Asn Asp Thr
-5 1 5
aga ctt tac cat gag gct gac aag acc tac atg tta cga gaa tat acg 147
Arg Leu Tyr His Glu Ala Asp Lys Thr Tyr Met Leu Arg Glu Tyr Thr
10 15 20
tca cga gaa agc aaa att tct agt ttg atg cat gtt cca cct tcc ctc 195
Ser Arg Glu Ser Lys Ile Ser Ser Leu Met His Val Pro Pro Ser Leu
25 30 35 40
ttc acg gaa cct aat gaa ata tcc cag tat tta cca ata aag gaa gca 243
Phe Thr Glu Pro Asn Glu Ile Ser Gln Tyr Leu Pro Ile Lys Glu Ala
45 50 55
gtt tgt gag aag cta ata ttt cca gaa aga att gat cct aac cca gca 291
Val Cys Glu Lys Leu Ile Phe Pro Glu Arg Ile Asp Pro Asn Pro Ala
60 65 70
gac tca caa aaa agt aca caa gtg gaa taaaatgtga tacaacatat 338
Asp Ser Gln Lys Ser Thr Gln Val Glu
75 80
actcactatg gaatctgact ggacaccttg gctatttgta aggggttatt tttattatga 398
gaattaattg ccttgtttat gtacagattt tctgtagcct taaaggaaaa aaaaataaag 458
atcgttacag gcaggtttca ctcaaaaaaa aaaaac 494

<210> 109
<211> 714
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 84..332

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<221> sig_peptide
<222> 84..170
<223> Von Heijne matrix
      score 5.2
      seq PCYYLGLFQRALA/SV

<221> polyA_site
<222> 702..714

<400> 109
cctatctctt ctgctggctg ggctcaatgc cgcgggtgag cgttcggccg aggctgctcc        60
taccottgag tgatgtgcct tga atg acg ctg ctt tca ttc gct gct ttc acg       113
                          Met Thr Leu Leu Ser Phe Ala Ala Phe Thr
                                          -25                 -20
gct gct ttc tcc gtc ctc ccc tgt tac tac ctt ggg ctg ttt cag cgg         161
Ala Ala Phe Ser Val Leu Pro Cys Tyr Tyr Leu Gly Leu Phe Gln Arg
            -15                 -10                 -5
gcg ctc gcg tcg gtc ttc gac cca ctt tgc gtt tgt tca cgt gtg ctc         209
Ala Leu Ala Ser Val Phe Asp Pro Leu Cys Val Cys Ser Arg Val Leu
            1               5                   10
ccg aca cct gta tgt acc ttg gtc gca aca caa gcc gaa aaa ata tta         257
Pro Thr Pro Val Cys Thr Leu Val Ala Thr Gln Ala Glu Lys Ile Leu
    15                  20                  25
gag aat ggg ccc tgt cca acc aag gag gcg gcc cag ctt gtc ggg aag         305
Glu Asn Gly Pro Cys Pro Thr Lys Glu Ala Ala Gln Leu Val Gly Lys
30                  35                  40                  45
ggc agc gtt tcc gcc aga aat gct tcg tgaaaggcac ttgagggacc               352
Gly Ser Val Ser Ala Arg Asn Ala Ser
                50
ttagcagcat cctcaacagg ccttgtaggg aatgccagaa gaagcagtcc ttggccgggc       412
ggggtggctc atgcctgtgg tcccagcact ttgggaggcc ggggcgggcg gatcacctga       472
ggtcgggagg tccagaccag cctgaccgac atggagaaac cccgtctnta ctagaaatac       532
aaaactagcc gggtgtggtg gcgcatgcct gtagtcccag ctactcggga gggtgaggca       592
ggagacgttc ttgaacccgg gaggcggagt ttgtggtgag ccgagatcgc gccattgcac       652
tccagcctgg gcatgccaag agcgaaactc cgtctcaaaa aaaaaaaaga aaaaaaaaaa       712
aa                                                                      714


<210> 110
<211> 805
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 32..718

<221> sig_peptide
<222> 32..100
<223> Von Heijne matrix
      score 7.4
      seq VLLLAALPPVLLP/GA

<221> polyA_signal
<222> 770..775

<221> polyA_site
<222> 793..805

<400> 110
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cctctttcag cccgggatcg ccccagcagg g atg ggc gac aag atc tgg ctg        52
                                   Met Gly Asp Lys Ile Trp Leu
                                                   -20
ccc ttc ccc gtg ctc ctt ctg gcc gct ctg cct ccg gtg ctg ctg cct      100
Pro Phe Pro Val Leu Leu Leu Ala Ala Leu Pro Pro Val Leu Leu Pro
    -15                 -10                 -5
ggg gcg gcc ggc ttc aca cct tcc ctc gat agc gac ttc acc ttt acc      148
Gly Ala Ala Gly Phe Thr Pro Ser Leu Asp Ser Asp Phe Thr Phe Thr
1               5                   10                  15
ctt ccc gcc ggc cag aag gag tgc ttc tac cag ccc atg ccc ctg aag      196
Leu Pro Ala Gly Gln Lys Glu Cys Phe Tyr Gln Pro Met Pro Leu Lys
            20                  25                  30
gcc tcg ctg gag atc gag tac caa gtt tta gat gga gca gga tta gat      244
Ala Ser Leu Glu Ile Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu Asp
        35                  40                  45
att gat ttc cat ctt gcc tct cca gaa ggc aaa acc tta gtt ttt gaa      292
Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe Glu
    50                  55                  60
caa aga aaa tca gat gga gtt cac act gta gag act gaa gtt ggt gat      340
Gln Arg Lys Ser Asp Gly Val His Thr Val Glu Thr Glu Val Gly Asp
65                  70                  75                  80
tac atg ttc tgc ttt gac aat aca ttc agc acc att tct gag aag gtg      388
Tyr Met Phe Cys Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Lys Val
                85                  90                  95
att ttc ttt gaa tta atc ctg gat aat atg gga gaa cag gca caa gaa      436
Ile Phe Phe Glu Leu Ile Leu Asp Asn Met Gly Glu Gln Ala Gln Glu
            100                 105                 110
caa gaa gat tgg aag aaa tat att act ggc aca gat ata ttg gat atg      484
Gln Glu Asp Trp Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp Met
        115                 120                 125
aaa ctg gaa gac atc ctg gaa tcc atc agc agc atc aag tcc aga cta      532
Lys Leu Glu Asp Ile Leu Glu Ser Ile Ser Ser Ile Lys Ser Arg Leu
    130                 135                 140
agc aaa agt ggg cac ata caa att ctg ctt aga gca ttt gaa gct cgt      580
Ser Lys Ser Gly His Ile Gln Ile Leu Leu Arg Ala Phe Glu Ala Arg
145                 150                 155                 160
gat cga aac ata caa gaa agc aac ttt gat aga gtc aat ttc tgg tct      628
Asp Arg Asn Ile Gln Glu Ser Asn Phe Asp Arg Val Asn Phe Trp Ser
                165                 170                 175
atg gtt aat tta gtg gtc atg gtg gtg gtg tca gcc att caa gtt tat      676
Met Val Asn Leu Val Val Met Val Val Val Ser Ala Ile Gln Val Tyr
            180                 185                 190
atg ctg aag agt ctg ttt gaa gat aag agg aaa agt aga act              718
Met Leu Lys Ser Leu Phe Glu Asp Lys Arg Lys Ser Arg Thr
        195                 200                 205
taaaactcca aactagagta cgtaacattg aaaaatgagg cataaaaatg caataaactg     778
ttacagtcaa gaccaaaaaa aaaaaaa                                         805
```

```
<210> 111
<211> 787
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 26..481

<221> sig_peptide
<222> 26..88
<223> Von Heijne matrix
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score 4.4
seq AVASSFFCASLFS/AV

<221> polyA_signal
<222> 755..760

<221> polyA_site
<222> 775..787

<400> 111
gacagcctgg ataaaggctc acttg atg gct cag ttg gga gca gtt gtg gct 52
Met Ala Gln Leu Gly Ala Val Val Ala
-20 -15
gtg gct tcc agt ttc ttt tgt gca tct ctc ttc tca gct gtg cac aag 100
Val Ala Ser Ser Phe Phe Cys Ala Ser Leu Phe Ser Ala Val His Lys
-10 -5 1
ata gaa gag gga cat att ggg gta tat tac aga ggc ggt gcc ctg ctg 148
Ile Glu Glu Gly His Ile Gly Val Tyr Tyr Arg Gly Gly Ala Leu Leu
5 10 15 20
act tcg acc agc ggc cct ggt ttc cat ctc atg ctc cct ttc atc aca 196
Thr Ser Thr Ser Gly Pro Gly Phe His Leu Met Leu Pro Phe Ile Thr
25 30 35
tca tat aag tct gtg cag acc aca ctc cag aca gat gag gtg aag aat 244
Ser Tyr Lys Ser Val Gln Thr Thr Leu Gln Thr Asp Glu Val Lys Asn
40 45 50
gta cct tgt ggg act agt ggt ggt gtg atg atc tac ttt gac aga att 292
Val Pro Cys Gly Thr Ser Gly Gly Val Met Ile Tyr Phe Asp Arg Ile
55 60 65
gaa gtg gtg aac ttc ctg gtc ccg aac gca gtg cat gat ata gtg aag 340
Glu Val Val Asn Phe Leu Val Pro Asn Ala Val His Asp Ile Val Lys
70 75 80
aac tat act gct gac tat gac aag gcc ctc atc ttc aac aag atc cac 388
Asn Tyr Thr Ala Asp Tyr Asp Lys Ala Leu Ile Phe Asn Lys Ile His
85 90 95 100
cac gaa ctg aac cag ttc tgc agt gtg cac acg ctt caa gag gtc tac 436
His Glu Leu Asn Gln Phe Cys Ser Val His Thr Leu Gln Glu Val Tyr
105 110 115
att gag ctg ttt gga ctg gaa aat gat ttt tcc cag gaa tct tca 481
Ile Glu Leu Phe Gly Leu Glu Asn Asp Phe Ser Gln Glu Ser Ser
120 125 130
taaaagggac cctgagcaag aacatttttc atagcagaca ggaggactca tccacatcgc 541
cagcaatcat aattaagcaa accgcctttt gcaccattta agatttagga aatcatccaa 601
attactttta atgtttctgc agtagaaaat gaatctaaat tcattttata gggtttgtag 661
tcttttatct gttttggatt cactgtgctt ttaagaaaaa gttggtaaat ttgccgttga 721
tttttctttt taacctcaaa ctaatagaat tttataaaat attaattttc tccaaaaaaa 781
aaaaaa 787

<210> 112
<211> 569
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 26..562

<221> sig_peptide
<222> 26..187
<223> Von Heijne matrix
score 4.1

seq AVVAAAARTGSEA/RV

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<400> 112
agaaacaggt ctgggctaca aaagt atg gcc gct tct gag gcg gcg gtg gtg        52
                            Met Ala Ala Ser Glu Ala Ala Val Val
                                            -50
tct tcg ccg tct ttg aaa aca gac aca tcc cct gtc ctt gaa act gca       100
Ser Ser Pro Ser Leu Lys Thr Asp Thr Ser Pro Val Leu Glu Thr Ala
-45                 -40                 -35                 -30
gga acg gtc gca gca atg gct gcg acc ccg tca gca agg gct gca gcc       148
Gly Thr Val Ala Ala Met Ala Ala Thr Pro Ser Ala Arg Ala Ala Ala
                -25                 -20                 -15
gcg gtg gtt gcg gcc gcg gcc agg acc gga tcc gaa gcc agg gtc tcc       196
Ala Val Val Ala Ala Ala Ala Arg Thr Gly Ser Glu Ala Arg Val Ser
            -10                 -5                  1
aag gcc gct ttg gct acc aag ctg ctg tcc ttg agc ggc gtg ttc gcc       244
Lys Ala Ala Leu Ala Thr Lys Leu Leu Ser Leu Ser Gly Val Phe Ala
    5                   10                  15
gtg cac aag ccc aaa ggg ccc act tca gcc gag ctg ctg aat cgg ttg       292
Val His Lys Pro Lys Gly Pro Thr Ser Ala Glu Leu Leu Asn Arg Leu
20                  25                  30                  35
aag gag aag ctg ctg gca gaa gct gga atg cct tct cca gaa tgg acc       340
Lys Glu Lys Leu Leu Ala Glu Ala Gly Met Pro Ser Pro Glu Trp Thr
                40                  45                  50
aag agg aaa aag cag act ttg aaa att ggg cat gga ggg act cta gac       388
Lys Arg Lys Lys Gln Thr Leu Lys Ile Gly His Gly Gly Thr Leu Asp
            55                  60                  65
agc gca gcc cga gga gtt ctg gtt gtt gga att gga agc gga aca aaa       436
Ser Ala Ala Arg Gly Val Leu Val Val Gly Ile Gly Ser Gly Thr Lys
        70                  75                  80
atg ttg acc agt atg ttg tca ggg tcc aag agg tat act gcc att gga       484
Met Leu Thr Ser Met Leu Ser Gly Ser Lys Arg Tyr Thr Ala Ile Gly
    85                  90                  95
gaa ctg ggg aaa gct act gat aca cta gat tct acg ggg aag gta aca       532
Glu Leu Gly Lys Ala Thr Asp Thr Leu Asp Ser Thr Gly Lys Val Thr
100                 105                 110                 115
gaa gaa aaa cct tac ggt atg aac ctc atc taagtag                       569
Glu Glu Lys Pro Tyr Gly Met Asn Leu Ile
                120                 125
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<210> 113
<211> 893
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 4..810

<221> sig_peptide
<222> 4..279
<223> Von Heijne matrix
      score 6.8
      seq AVMLYTWRSCSRA/IP

<221> polyA_signal
<222> 858..863

<221> polyA_site
<222> 881..893
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<400> 113

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gcc atg atc acg cac gtc acc ctg gaa gat gcc ctg tcc aac gtg gac        48
    Met Ile Thr His Val Thr Leu Glu Asp Ala Leu Ser Asn Val Asp
            -90                 -85                 -80
ctg ctt gaa gag ctt ccc ctc ccc gac cag cag cca tgc atc gag cct        96
Leu Leu Glu Glu Leu Pro Leu Pro Asp Gln Gln Pro Cys Ile Glu Pro
        -75                 -70                 -65
cca cct tcc tcc atc atg tac cag gct aac ttt gac aca aac ttt gag       144
Pro Pro Ser Ser Ile Met Tyr Gln Ala Asn Phe Asp Thr Asn Phe Glu
    -60                 -55                 -50
gac agg aat gca ttt gtc acg ggc att gca agg tac att gag cag gct       192
Asp Arg Asn Ala Phe Val Thr Gly Ile Ala Arg Tyr Ile Glu Gln Ala
-45                 -40                 -35                 -30
aca gtc cac tcc agc atg aat gag atg ctg gag gaa gga cat gag tat       240
Thr Val His Ser Ser Met Asn Glu Met Leu Glu Glu Gly His Glu Tyr
                -25                 -20                 -15
gcg gtc atg ctg tac acc tgg cgc agc tgt tcc cgg gcc att ccc cag       288
Ala Val Met Leu Tyr Thr Trp Arg Ser Cys Ser Arg Ala Ile Pro Gln
            -10                 -5                  1
gtg aaa tgc aac gag cag ccc aac cga gta gag atc tat gag aag aca       336
Val Lys Cys Asn Glu Gln Pro Asn Arg Val Glu Ile Tyr Glu Lys Thr
    5                   10                  15
gta gag gtg ctg gag ccg gag gtc acc aag ctc atg aag ttc atg tat       384
Val Glu Val Leu Glu Pro Glu Val Thr Lys Leu Met Lys Phe Met Tyr
20                  25                  30                  35
ttt cag cgc aag gcc atc gag cgg ttc tgc agc gag gtg aag cgg ctg       432
Phe Gln Arg Lys Ala Ile Glu Arg Phe Cys Ser Glu Val Lys Arg Leu
                40                  45                  50
tgc cat gcc gag cgc agg aag gac ttt gtc tct gag gcc tac ctc ctg       480
Cys His Ala Glu Arg Arg Lys Asp Phe Val Ser Glu Ala Tyr Leu Leu
            55                  60                  65
acc ctt ggc aag ttc atc aac atg ttt gct gtc ctg gat gag cta aag       528
Thr Leu Gly Lys Phe Ile Asn Met Phe Ala Val Leu Asp Glu Leu Lys
        70                  75                  80
aac atg aag tgc agc gtc aag aat gac cac tcc gcc tac aag agg gca       576
Asn Met Lys Cys Ser Val Lys Asn Asp His Ser Ala Tyr Lys Arg Ala
    85                  90                  95
gca cag ttc ctg cgg aag atg gca gat ccc cag tct atc cag gag tcg       624
Ala Gln Phe Leu Arg Lys Met Ala Asp Pro Gln Ser Ile Gln Glu Ser
100                 105                 110                 115
cag aac ctt tcc atg ttc ctg gcc aac cac aac agg atc acc cag tgt       672
Gln Asn Leu Ser Met Phe Leu Ala Asn His Asn Arg Ile Thr Gln Cys
                120                 125                 130
ctc cac cag caa ctt gaa gtg atc cca ggc tat gag gag ctg ctg gct       720
Leu His Gln Gln Leu Glu Val Ile Pro Gly Tyr Glu Glu Leu Leu Ala
            135                 140                 145
gac att gtc aac atc tgt gtg gat tac tac gag aac aag atg tac ctg       768
Asp Ile Val Asn Ile Cys Val Asp Tyr Tyr Glu Asn Lys Met Tyr Leu
        150                 155                 160
act ccc agt gag aaa cat atg ctc ctc aag gta aaa ctc ccc               810
Thr Pro Ser Glu Lys His Met Leu Leu Lys Val Lys Leu Pro
    165                 170                 175
tgaggccgca cccatggagc ctgggcttac cctctcacct tcttcttatt aaaaatccgt     870
tttaaaaaac aaaaaaaaaa aaa                                             893
```

<210> 114
<211> 1475
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 55..459

<221> sig_peptide
<222> 55..120
<223> Von Heijne matrix
score 7.2
seq GLWLALVDGLVRS/SP

<221> polyA_signal
<222> 1444..1449

<221> polyA_site
<222> 1462..1475

<400> 114
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cagttccgca gctacgtgtg ggacccgctg ctgatcctgt cgcagatcgt cctc atg       57
                                                            Met
cag acc gtg tat tac ggc tcg ctg ggc ctg tgg ctg gcg ctg gtg gac      105
Gln Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val Asp
    -20                 -15                 -10
ggg cta gtg cga agc agc ccc tcg ctg gac cag atg ttc gac gcc gag      153
Gly Leu Val Arg Ser Ser Pro Ser Leu Asp Gln Met Phe Asp Ala Glu
-5                  1               5                   10
atc ctg ggc ttt tcc acc cct cca ggc cgg ctc tcc atg atg tcc ttc      201
Ile Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser Phe
            15                  20                  25
atc ttc aac gcc ctc acc tgt gcc ctg ggc ttg ctg tac ttc atc cgg      249
Ile Phe Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile Arg
        30                  35                  40
cga gga aag cag tgt ctg gat ttc act gtc act gtc cat ttc ttt cac      297
Arg Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His
    45                  50                  55
ctc ctg ggc tgc tgg ttc tac agc tcc cgt ttc ccc tcg gcg ctg acc      345
Leu Leu Gly Cys Trp Phe Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr
60                  65                  70                  75
tgg tgg ctg gtc caa gcc gtg tgc att gca ctc atg gct gtc atc ggg      393
Trp Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile Gly
                80                  85                  90
gag tac ctg tgc atg cgg acg gag ctc aag gag ata ccc ctc aac tca      441
Glu Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Asn Ser
            95                  100                 105
gcc cct aaa tcc aat gtc tagaatcagg ccctttggac atcccgctga            489
Ala Pro Lys Ser Asn Val
        110
cacttgggcc ccttaacacc ttgggctgct cagaccctcc agatgaggtc cagcccagat    549
ctgagaggaa ccctggaaat gtgaagtctc tgttggtgtg ggagagatag tgagggcctg    609
tcaaagaagg caggtagcag tcagcatgac agctgcaaga atgacctctg tctgttgaag    669
ccttggtatc tgagaggtca ggaaggggac ctctttgagg gtaataacat aattggaacc    729
atgccactct tgagccacaa tacctgtcac cagcctgttg ttttaagaga gaaaaaaaat    789
caaggatatc tgattggagc aaaccacttc tttagtcatc tgtcttacct ccctgggaca    849
gctgttacct ttgcagtgtt gccgaatcac agcagttacc tttgcaatgt tgccgaatca    909
cagcagttct gttggagaaa cgcttggttt ccggatccag agccacagaa agaaatgtag    969
gtgtgaagta ttaggctgct gtcagggaga ggatggcaga tggaggcatc aagcacaagg   1029
aaaatgcaca acctgtgccc tgttatacac acgttcatgt gcgcccaaga acctatgact   1089
ttcttccagt tccttctacc aggtccccat cctgctgcca gctctcaaca tagcaggcca   1149
taggacccag agaagaatcc cagtgttgct caaagtctga ccatcataaa gacactgcct   1209
gtcttctagg aatgaccagg cacccagctc ccactggact ccaatttttt ttcctgcctt   1269
atttagaatt ctttggcggg aagggtatga tgggttccca gagacaagaa gcccaacctt   1329
ctggcctggg ctgtgctgat agtgctgagg gagataggaa tttgctgcta agatttttct   1389
```

```
ttggggtgga gtttcctctg tgaggggctt gcagctatcc ttcctgtgta tacaaataca    1449
gtattttcca tgaaaaaaaa aaaaaa                                          1475



<210> 115
<211> 321
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 48..248

<221> sig_peptide
<222> 48..161
<223> Von Heijne matrix
      score 6.3
      seq LVFALVTAVCCLA/DG

<221> polyA_signal
<222> 283..288

<221> polyA_site
<222> 308..321

<400> 115
gctgagaaga gttgagggaa agtgctgctg ctgggtctgc agacgcg atg aat aac        56
                                                    Met Asn Asn
gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg aaa ggc       104
Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val Lys Gly
-35                 -30                 -25                 -20
cac gtg aag atg ctg cgg ctg gtg ttt gca ctt gtg aca gca gta tgc       152
His Val Lys Met Leu Arg Leu Val Phe Ala Leu Val Thr Ala Val Cys
                -15                 -10                  -5
tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc aat ccc       200
Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe Asn Pro
             1               5                  10
aac ggt cct tac cag aaa aag cct gtg cat gaa aaa aaa gaa gtt ttg       248
Asn Gly Pro Tyr Gln Lys Lys Pro Val His Glu Lys Lys Glu Val Leu
    15                  20                  25
tgattttata ttacttttta gtttgatact aagtattaaa catatttctg tattcttcca     308
aaaaaaaaaa aaa                                                        321



<210> 116
<211> 450
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 25..399

<221> sig_peptide
<222> 25..186
<223> Von Heijne matrix
      score 3.5
      seq SILAQVLDQSARA/RL

<400> 116
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ctgctccagc gctgacgccg agcc atg gcg gac gag gag ctt gag gcg ctg          51
                           Met Ala Asp Glu Glu Leu Glu Ala Leu
                                           -50
agg aga cag agg ctg gcc gag ctg cag gcc aaa cac ggg gat cct ggt         99
Arg Arg Gln Arg Leu Ala Glu Leu Gln Ala Lys His Gly Asp Pro Gly
-45                 -40                 -35                 -30
gat gcg gcc caa cag gaa gca aag cac agg gaa gca gaa atg aga aac        147
Asp Ala Ala Gln Gln Glu Ala Lys His Arg Glu Ala Glu Met Arg Asn
                -25                 -20                 -15
agt atc tta gcc caa gtt ctg gat cag tcg gcc cgg gcc agg tta agt        195
Ser Ile Leu Ala Gln Val Leu Asp Gln Ser Ala Arg Ala Arg Leu Ser
            -10                  -5                   1
aac tta gca ctt gta aag cct gaa aaa act aaa gca gta gag aat tac        243
Asn Leu Ala Leu Val Lys Pro Glu Lys Thr Lys Ala Val Glu Asn Tyr
      5                  10                  15
ctt ata cag atg gca aga tat gga caa cta agt gag aag gta tca gaa        291
Leu Ile Gln Met Ala Arg Tyr Gly Gln Leu Ser Glu Lys Val Ser Glu
20                  25                  30                  35
caa ggt tta ata gaa atc ctt aaa aaa gta agc caa caa aca gaa aag        339
Gln Gly Leu Ile Glu Ile Leu Lys Lys Val Ser Gln Gln Thr Glu Lys
                40                  45                  50
aca aca aca gtg aaa ttc aac aga aga aaa gta atg gac tct gat gaa        387
Thr Thr Thr Val Lys Phe Asn Arg Arg Lys Val Met Asp Ser Asp Glu
            55                  60                  65
gat gac gat tat tgaactacaa gtgctcacag actagaactt aacggaacaa            439
Asp Asp Asp Tyr
        70
gtctaggaca g                                                           450
```

<210> 117
<211> 1173
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 10..1137

<221> sig_peptide
<222> 10..72
<223> Von Heijne matrix
score 6.5
seq LLTLLLPPPPLYT/RH

<221> polyA_signal
<222> 1144..1149

<221> polyA_site
<222> 1162..1173

<400> 117

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gagctgctt atg gga cac cgc ttc ctg cgc ggc ctc tta acg ctg ctg ctg       51
          Met Gly His Arg Phe Leu Arg Gly Leu Leu Thr Leu Leu Leu
              -20                 -15                 -10
ccg ccg cca ccc ctg tat acc cgg cac cgc atg ctc ggt cca gag tcc         99
Pro Pro Pro Pro Leu Tyr Thr Arg His Arg Met Leu Gly Pro Glu Ser
         -5                   1                   5
gtc ccg ccc cca aaa cga tcc cgc agc aaa ctc atg gca ccg ccc cga        147
Val Pro Pro Pro Lys Arg Ser Arg Ser Lys Leu Met Ala Pro Pro Arg
10                  15                  20                  25
```

atc ggg acg cac aat ggc acc ttc cac tgc gac gag gca ctg gca tgc 195
Ile Gly Thr His Asn Gly Thr Phe His Cys Asp Glu Ala Leu Ala Cys
30 35 40

gca ctg ctt cgc ctc ctg ccg gag tac cgg gat gca gag att gtg cgg 243
Ala Leu Leu Arg Leu Leu Pro Glu Tyr Arg Asp Ala Glu Ile Val Arg
45 50 55

acc cgg gat ccc gaa aaa ctc gct tcc tgt gac atc gtg gtg gac gtg 291
Thr Arg Asp Pro Glu Lys Leu Ala Ser Cys Asp Ile Val Val Asp Val
60 65 70

ggg ggc gag tac gac cct cgg aga cac cga tat gac cat cac cag agg 339
Gly Gly Glu Tyr Asp Pro Arg Arg His Arg Tyr Asp His His Gln Arg
75 80 85

tct ttc aca gag acc atg agc tcc ctg tcc cct ggg agg ccg tgg cag 387
Ser Phe Thr Glu Thr Met Ser Ser Leu Ser Pro Gly Arg Pro Trp Gln
90 95 100 105

acc aag ctg agc agt gcg gga ctc atc tat ctg cac ttc ggg cac aag 435
Thr Lys Leu Ser Ser Ala Gly Leu Ile Tyr Leu His Phe Gly His Lys
110 115 120

ctg ctg gcc cag ttg ctg ggc act agt gaa gag gac agc atg gtg ggc 483
Leu Leu Ala Gln Leu Leu Gly Thr Ser Glu Glu Asp Ser Met Val Gly
125 130 135

acc ctc tat gac aag atg tat gag aac ttt gtg gag gag gtg gat gct 531
Thr Leu Tyr Asp Lys Met Tyr Glu Asn Phe Val Glu Glu Val Asp Ala
140 145 150

gtg gac aat ggg atc tcc cag tgg gca gag ggg gag cct cga tat gca 579
Val Asp Asn Gly Ile Ser Gln Trp Ala Glu Gly Glu Pro Arg Tyr Ala
155 160 165

ctg acc act acc ctg agt gca cga gtt gct cga ctt aat cct acc tgg 627
Leu Thr Thr Thr Leu Ser Ala Arg Val Ala Arg Leu Asn Pro Thr Trp
170 175 180 185

aac cac ccc gac caa gac act gag gca ggg ttc aag cgt gca atg gat 675
Asn His Pro Asp Gln Asp Thr Glu Ala Gly Phe Lys Arg Ala Met Asp
190 195 200

ctg gtt caa gag gag ttt ctg cag aga tta gat ttc tac caa cac agc 723
Leu Val Gln Glu Glu Phe Leu Gln Arg Leu Asp Phe Tyr Gln His Ser
205 210 215

tgg ctg cca gcc cgg gcc ttg gtg gaa gag gcc ctt gcc cag cga ttc 771
Trp Leu Pro Ala Arg Ala Leu Val Glu Glu Ala Leu Ala Gln Arg Phe
220 225 230

cag gtg gac cca agt gga gag att gtg gaa ctg gcg aaa ggt gca tgt 819
Gln Val Asp Pro Ser Gly Glu Ile Val Glu Leu Ala Lys Gly Ala Cys
235 240 245

ccc tgg aag gag cat ctc tac cac ctg gaa tct ggg ctg tcc cct cca 867
Pro Trp Lys Glu His Leu Tyr His Leu Glu Ser Gly Leu Ser Pro Pro
250 255 260 265

gtg gcc atc ttc ttt gtt atc tac act gac cag gct gga cag tgg cga 915
Val Ala Ile Phe Phe Val Ile Tyr Thr Asp Gln Ala Gly Gln Trp Arg
270 275 280

ata cag tgt gtg ccc aag gag ccc cac tca ttc caa agc cgg ctg ccc 963
Ile Gln Cys Val Pro Lys Glu Pro His Ser Phe Gln Ser Arg Leu Pro
285 290 295

ctg cca gag cca tgg cgg ggt ctt cgg gac gag gcc ctg gac cag gtc 1011
Leu Pro Glu Pro Trp Arg Gly Leu Arg Asp Glu Ala Leu Asp Gln Val
300 305 310

agt ggg atc cct ggc tgc atc ttc gtc cat gca agc ggc ttc att ggc 1059
Ser Gly Ile Pro Gly Cys Ile Phe Val His Ala Ser Gly Phe Ile Gly
315 320 325

ggt cac cgc acc cga gag ggt gcc ttg agc atg gcc cgt gcc acc ttg 1107
Gly His Arg Thr Arg Glu Gly Ala Leu Ser Met Ala Arg Ala Thr Leu
330 335 340 345

gcc cag cgc tca tac ctc cca caa atc tcc tagtctaata aaaccttcca 1157
Ala Gln Arg Ser Tyr Leu Pro Gln Ile Ser

350 355
tctcaaaaaa aaaaaa 1173

<210> 118
<211> 785
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 72..704

<221> sig_peptide
<222> 72..161
<223> Von Heijne matrix
score 13.2
seq LLLLSTLVIPSAA/AP

<221> polyA_signal
<222> 772..777

<400> 118
cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga 60
aggggcgggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat 110
Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His
-30 -25 -20

ctg ctg gtc ctg ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct 158
Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala
-15 -10 -5

gca gct cct atc cat gat gct gac gcc caa gag agc tcc ttg ggt ctc 206
Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu
1 5 10 15

aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa 254
Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys
20 25 30

ggt aac ctg ctt cgg ggc ata gac agc tta ttc tct gcc ccc atg gac 302
Gly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp
35 40 45

ttc cgg ggc ctc cct ggg aac tac cac aaa gag gag aac cag gag cac 350
Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His
50 55 60

cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta 398
Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val
65 70 75

ccc agg atg gag gag aag gag gcc ctg gta ccc atc cag aag gcc acg 446
Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr
80 85 90 95

gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att 494
Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile
100 105 110

aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 542
Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His
115 120 125

tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc 590
Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu
130 135 140

cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638
Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser
145 150 155

tcc cac tcc agg ctg tcc ccc cga aag acc cac tta ctg tac atc ctc 686

```
Ser His Ser Arg Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu
160                 165                 170                 175
agg ccc tct cgg cag ctg taggggtggg gaccggggag cacctgcctg          734
Arg Pro Ser Arg Gln Leu
                180
tagcccccat cagaccctgc cccaagcacc atatggaaat aaagttcttt c          785
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<210> 119
<211> 559
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 44..505

<221> sig_peptide
<222> 44..223
<223> Von Heijne matrix
      score 4
      seq LVRRTLLVAALRA/WM

<400> 119

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agcaaccaga gggagatgat cacctgaacc actgctccaa acc atg ggc agt aaa        55
                                                Met Gly Ser Lys
                                                -60
tgc tgt aaa ggt ggt cca gat gaa gat gca gta gaa aga cag agg cgg       103
Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu Arg Gln Arg Arg
    -55                 -50                 -45
cag aag ttg ctt ctt gca caa ctg cat cac aga aaa agg gtg aag gca       151
Gln Lys Leu Leu Leu Ala Gln Leu His His Arg Lys Arg Val Lys Ala
-40                 -35                 -30                 -25
gct ggg cag atc cag gcc tgg tgg cgt ggg gtc ctg gtg cgc agg acc       199
Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu Val Arg Arg Thr
                -20                 -15                 -10
ctg ctg gtt gct gcc ctc agg gcc tgg atg att cag tgc tgg tgg agg       247
Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln Cys Trp Trp Arg
            -5                  1               5
acg ttg gtg cag aga cgg atc cgt cag cgg cgg cag gcc ctg ttg agg       295
Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln Ala Leu Leu Arg
    10                  15                  20
gtc tac gtc atc cag gag cag gcg acg gtc aag ctc cag tcc tgc atc       343
Val Tyr Val Ile Gln Glu Gln Ala Thr Val Lys Leu Gln Ser Cys Ile
25                  30                  35                  40
cgc atg tgg cag tgc cgg caa tgt tac cgc caa atg tgc aat gct ctc       391
Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met Cys Asn Ala Leu
                45                  50                  55
tgc ttg ttc cag gtc cca gag agc agc ctt gcc ttc cag act gat ggc       439
Cys Leu Phe Gln Val Pro Glu Ser Ser Leu Ala Phe Gln Thr Asp Gly
            60                  65                  70
ttt tta cag gtc caa tat gca atc cct tca aag cag cca gag ttc cac       487
Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu Phe His
        75                  80                  85
att gaa atc cta tca atc tgaaaggcct ggggcatgga gaacaggctg              535
Ile Glu Ile Leu Ser Ile
    90
cactacccta ataaatgtct gacc                                            559
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<210> 120
<211> 770
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 25..393

<221> sig_peptide
<222> 25..150
<223> Von Heijne matrix
      score 4.6
      seq LDPAVSLSAPAFA/SA

<221> polyA_signal
<222> 734..739

<221> polyA_site
<222> 757..770

<400> 120
cgcagaaagg agagacacac atac atg aaa gga gga gct ttc tcc aat ctt     51
                           Met Lys Gly Gly Ala Phe Ser Asn Leu
                                   -40                 -35
aat gat tcc cag ctc tca gcc tcg ttt ctg caa ccc agc ctg caa gca    99
Asn Asp Ser Gln Leu Ser Ala Ser Phe Leu Gln Pro Ser Leu Gln Ala
        -30                 -25                 -20
aac tgt cct gct ttg gac cct gct gtg tca ctc tcc gca cca gcc ttt   147
Asn Cys Pro Ala Leu Asp Pro Ala Val Ser Leu Ser Ala Pro Ala Phe
    -15                 -10                 -5
gcc tct gct ctt cgc tct atg aag tcc tcc cag gct gca cgg aag gac   195
Ala Ser Ala Leu Arg Ser Met Lys Ser Ser Gln Ala Ala Arg Lys Asp
  1               5                  10                  15
gac ttt ctc agg tct ctt agt gat gga gac tca ggg aca tca gaa cac   243
Asp Phe Leu Arg Ser Leu Ser Asp Gly Asp Ser Gly Thr Ser Glu His
                20                  25                  30
atc tca gcg gtg gtg act agc cct cgg att tcc tgc cat ggt gct gcc   291
Ile Ser Ala Val Val Thr Ser Pro Arg Ile Ser Cys His Gly Ala Ala
            35                  40                  45
att ccc acc gcc cgt gcc ctc tgc cta ggc tgt tcc tgc tgc acc gaa   339
Ile Pro Thr Ala Arg Ala Leu Cys Leu Gly Cys Ser Cys Cys Thr Glu
        50                  55                  60
cgc ctc ctc ctg cca ccg ccc tcc ctc ctt tct tta gaa gcc cct gcc   387
Arg Leu Leu Leu Pro Pro Pro Ser Leu Leu Ser Leu Glu Ala Pro Ala
    65                  70                  75
agc acc tgagctctct gctgattgct gttcctccca gtctgtggaa gctttgccca    443
Ser Thr
80
tatgctttcc ttaaaagggt tctgggcagg gcaggcgccc ccatttctca gggatcccct   503
ccaggacaac gccttttcct tgtgtcttca gctctcctta ccagatatct atatatttgt   563
atatattcag tttcaccaac aatgcatcaa gtactttttt ttttaagtaa agaaccgcag   623
tcatcgaact ggagccccat tgattccctc cccctcgcct ccccaaatct ggcacctgcc   683
caaggtatcc tcagaaccat ttggggtgtc ctttggcatt ggataataga aataaaattt   743
tacctctttc tacaaaaaaa aaaaaac                                       770


<210> 121
<211> 1213
<212> DNA
<213> Homo sapiens
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<220>
<221> CDS
<222> 58..1095

<221> sig_peptide
<222> 58..114
<223> Von Heijne matrix
score 5.4
seq LSHLLPSLRQVIQ/EP

<221> polyA_site
<222> 1202..1213

<400> 121
cctggctttg cctttgccct gctgtgtgat cttagctccc tgcccaggcc cacagcc 57
atg gcc atg gcc cag aaa ctc agc cac ctc ctg ccg agt ctg cgg cag 105
Met Ala Met Ala Gln Lys Leu Ser His Leu Leu Pro Ser Leu Arg Gln
-15 -10 -5
gtc atc cag gag cct cag cta tct ctg cag cca gag cct gtc ttc acg 153
Val Ile Gln Glu Pro Gln Leu Ser Leu Gln Pro Glu Pro Val Phe Thr
1 5 10
gtg gat cga gct gag gtg ccg ccg ctc ttc tgg aag ccg tac atc tat 201
Val Asp Arg Ala Glu Val Pro Pro Leu Phe Trp Lys Pro Tyr Ile Tyr
15 20 25
gcg ggc tac cgg ccg ctg cat cag acc tgg cgc ttc tat ttc cgc acg 249
Ala Gly Tyr Arg Pro Leu His Gln Thr Trp Arg Phe Tyr Phe Arg Thr
30 35 40 45
ctg ttc cag cag cac aac gag gcc gtg aat gtc tgg acc cac ctg ctg 297
Leu Phe Gln Gln His Asn Glu Ala Val Asn Val Trp Thr His Leu Leu
50 55 60
gcg gcc ctg gta ctg ctg ctg cgg ctg gcc ctc ttt gtg gag acc gtg 345
Ala Ala Leu Val Leu Leu Leu Arg Leu Ala Leu Phe Val Glu Thr Val
65 70 75
gac ttc tgg gga gac cca cac gcc ctg ccc ctc ttc atc att gtc ctt 393
Asp Phe Trp Gly Asp Pro His Ala Leu Pro Leu Phe Ile Ile Val Leu
80 85 90
gcc tct ttc acc tac ctc tcc ctc agt gcc ttg gct cac ctc ctg cag 441
Ala Ser Phe Thr Tyr Leu Ser Leu Ser Ala Leu Ala His Leu Leu Gln
95 100 105
gcc aag tct gag ttc tgg cat tac agc ttc ttc ttc ctg gac tat gtg 489
Ala Lys Ser Glu Phe Trp His Tyr Ser Phe Phe Phe Leu Asp Tyr Val
110 115 120 125
ggg gtg gcc gtg tac cag ttt ggc agt gcc ttg gca cac ttc tac tat 537
Gly Val Ala Val Tyr Gln Phe Gly Ser Ala Leu Ala His Phe Tyr Tyr
130 135 140
gct atc gag ccc gcc tgg cat gcc cag gtg cag gct gtt ttt ctg ccc 585
Ala Ile Glu Pro Ala Trp His Ala Gln Val Gln Ala Val Phe Leu Pro
145 150 155
atg gct gcc ttt ctc gcc tgg ctt tcc tgc att ggc tcc tgc tat aac 633
Met Ala Ala Phe Leu Ala Trp Leu Ser Cys Ile Gly Ser Cys Tyr Asn
160 165 170
aag tac atc cag aaa cca ggc ctg ctg ggc cgc aca tgc cag gag gtg 681
Lys Tyr Ile Gln Lys Pro Gly Leu Leu Gly Arg Thr Cys Gln Glu Val
175 180 185
ccc tcc gtc ctg gcc tac gca ctg gac att agt cct gtg gtg cat cgt 729
Pro Ser Val Leu Ala Tyr Ala Leu Asp Ile Ser Pro Val Val His Arg
190 195 200 205
atc ttc gtg tcc tcc gac ccc acc acg gat gat cca gct ctt ctc tac 777
Ile Phe Val Ser Ser Asp Pro Thr Thr Asp Asp Pro Ala Leu Leu Tyr
210 215 220
cac aag tgc cag gtg gtc ttc ttt ctg ctg gct gct gcc ttc ttc tct 825

```
His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Ala Phe Phe Ser
        225                 230                 235
acc ttc atg ccc gag cgc tgg ttc cct ggc agc tgc cat gtc ttc ggg      873
Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly
    240                 245                 250
cag ggc cac caa ctt ttc cat atc ttc ttg gtg ctg tgc acg ctg gct      921
Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala
    255                 260                 265
cag ctg gag gct gtg gca ctg gac tat gag gcc cga cgg ccc atc tat      969
Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr
270                 275                 280                 285
gag cct ctg cac acg cac tgg cct cac aac ttt tct ggc ctc ttc ctg     1017
Glu Pro Leu His Thr His Trp Pro His Asn Phe Ser Gly Leu Phe Leu
                290                 295                 300
ctc acg gtg ggc agc agc atc ctc act gca ttc ctc ctg agc cag ctg     1065
Leu Thr Val Gly Ser Ser Ile Leu Thr Ala Phe Leu Leu Ser Gln Leu
            305                 310                 315
gta cag cgc aaa ctt gat cag aag acc aag tgaaggggga tggcatctgg       1115
Val Gln Arg Lys Leu Asp Gln Lys Thr Lys
        320                 325
tagggaggga ggtatagttg ggggacaggg gtctgggttt ggctccaagt gggaacaagg  1175
cctggtaaag ttgtttgtgt ctggccaaaa aaaaaaa                           1213
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<210> 122
<211> 1318
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 31..660

<221> sig_peptide
<222> 31..90
<223> Von Heijne matrix
score 5.4
seq AFVIACVLSLIST/IY

<221> polyA_signal
<222> 1288..1293

<221> polyA_site
<222> 1307..1318

<400> 122

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ggaggatggg cgagcagtct gaatgccaga atg gat aac cgt ttt gct aca gca      54
                                 Met Asp Asn Arg Phe Ala Thr Ala
                                 -20                 -15
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca     102
Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala
        -10                 -5                  1
gct tcc att ggc aca gac ttc tgg tat gag tat cga agt cca gtt caa     150
Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln
5                   10                  15                  20
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt     198
Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser
                25                  30                  35
gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat     246
Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn
            40                  45                  50
```

ggc aca gtg gga ttg tgg aga cgg tgt atc acc ata ccc aaa aac atg 294
Gly Thr Val Gly Leu Trp Arg Arg Cys Ile Thr Ile Pro Lys Asn Met
55 60 65

cat tgg tat agc cca cca gaa agg aca gag tca ttt gat gtg gtc aca 342
His Trp Tyr Ser Pro Pro Glu Arg Thr Glu Ser Phe Asp Val Val Thr
70 75 80

aaa tgt gtg agt ttc aca cta act gag cag ttc atg gag aaa ttt gtt 390
Lys Cys Val Ser Phe Thr Leu Thr Glu Gln Phe Met Glu Lys Phe Val
85 90 95 100

gat ccc gga aac cac aat agc ggg att gat ctc ctt agg acc tat ctt 438
Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu Leu Arg Thr Tyr Leu
105 110 115

tgg cgt tgc cag ttc ctt tta cct ttt gtg agt tta ggt ttg atg tgc 486
Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser Leu Gly Leu Met Cys
120 125 130

ttt ggg gct ttg atc gga ctt tgt gct tgc att tgc cga agc tta tat 534
Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile Cys Arg Ser Leu Tyr
135 140 145

ccc acc att gcc acg ggc att ctc cat ctc ctt gca gtg aca aag gag 582
Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu Ala Val Thr Lys Glu
150 155 160

agc atg ctt cca gct gga gct gag tcc aag cac aca gcc act cct gca 630
Ser Met Leu Pro Ala Gly Ala Glu Ser Lys His Thr Ala Thr Pro Ala
165 170 175 180

cac gca tgc gtg caa aca ggg aag ccc aag taggagaaga ggaaagaggt 680
His Ala Cys Val Gln Thr Gly Lys Pro Lys
185 190

tgtagggatt tgggaagaac cttgattatt ccctggagga aaagacaaat ctacttccct 740
gaaatcaccc tcgaatctac ttccaccctc agaacttaaa atgaactgca tcctttttt 800
catcttcttt tcttctccag tgaatatgat ctccaaaccc ttatttttc tttgaactgt 860
aaaatttcca ctcatggacg atgcaaccaa cagatgcaat ctctgagaag atgaaaattg 920
ggacctctta ttataaaatt gacctagctg gactcaggaa accagggaag aagtcaatgc 980
aggcatttaa aatgtaaagt tttttctggt taaatctatt tatttttctt gtaggttgag 1040
tatttcttcc cagtttttct gctctggtgt ataacaaaca ggtcaaaatt tcccatcttt 1100
cctcctgata gtagttgaat cctacccttgc atacttaatg catagtgaaa tggcatctag 1160
cagaaataca cacccccaaa acacaccacc atttcattag gtgcccaaaa aattctgtat 1220
ttagcttatt tatttattgt tatttttgct ttttcttaac ccactatata ttgactgcaa 1280
acgaattaat aaattatccc ttctggaaaa aaaaaaaa 1318

<210> 123
<211> 853
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 31..582

<221> sig_peptide
<222> 31..90
<223> Von Heijne matrix
score 5.4
seq AFVIACVLSLIST/IY

<221> polyA_signal
<222> 816..821

<221> polyA_site
<222> 840..853

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<400> 123
ggaggatggg cgagcagtct gaatgccaga atg gat aac cgt ttt gct aca gca      54
                                 Met Asp Asn Arg Phe Ala Thr Ala
                                 -20                 -15
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca      102
Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala
        -10                 -5                  1
gcc tcc att ggc aca gac ttc tgg tat gaa tat cga agt cca gtt caa      150
Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln
5                   10                  15                  20
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt      198
Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser
                25                  30                  35
gat gaa gca gat gaa aag act tat aat gat gca cct ttt cga tac aat      246
Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Pro Phe Arg Tyr Asn
            40                  45                  50
ggc aca gtg gga ttg tgg aga cgg tgt atc acc ata ccc aaa aac atg      294
Gly Thr Val Gly Leu Trp Arg Arg Cys Ile Thr Ile Pro Lys Asn Met
        55                  60                  65
cat tgg tat agc cca cca gaa agg aca gag tca ttt gat gtg gtc aca      342
His Trp Tyr Ser Pro Pro Glu Arg Thr Glu Ser Phe Asp Val Val Thr
    70                  75                  80
aaa tgt gtg agt ttc aca cta act gag cag ttc atg gag aaa ttt gtt      390
Lys Cys Val Ser Phe Thr Leu Thr Glu Gln Phe Met Glu Lys Phe Val
85                  90                  95                  100
gat ccc gga aac cac aat agc ggg att gat ctc ctt agg acc tat ctt      438
Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu Leu Arg Thr Tyr Leu
                105                 110                 115
tgg cgt tgc cag ttc ctt tta cct ttt gtg agt tta ggt ttg atg tgc      486
Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser Leu Gly Leu Met Cys
            120                 125                 130
ttt ggg gct ttg atc gga ctt tgt gct tgc att tgc cga agc tta tat      534
Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile Cys Arg Ser Leu Tyr
        135                 140                 145
ccc acc att gcc acg ggc att ctc cat ctc ctt gca gat acc atg ctg      582
Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu Ala Asp Thr Met Leu
    150                 155                 160
tgaagtccag gccacatgga ggtgtcctgt gtagatgctc cagctgaaat cccaagctaa    642
gctcccaact gacagccaac atcatttcca gccatgtgtg ggagccatcc tggatgtcca    702
gccttaacaa gccttcagag gacttcagcc acagctatta tcttactaca tccttgtgag    762
actctaataa agaaccaact agctgagccc aatcaaccta tggaactgat agaaataaaa    822
tgaattgttg ttttgcgaaa aaaaaaaaaa a                                   853


<210> 124
<211> 826
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 15..695

<221> sig_peptide
<222> 15..80
<223> Von Heijne matrix
      score 8.5
      seq AALLLGLMMVVTG/DE

<221> polyA_signal
<222> 795..800
```

<221> polyA_site
<222> 814..826

<400> 124
aaccagaggt gccc atg ggt tgg aca atg agg ctg gtc aca gca gca ctg 50
Met Gly Trp Thr Met Arg Leu Val Thr Ala Ala Leu
-20 -15
tta ctg ggt ctc atg atg gtg gtc act gga gac gag gat gag aac agc 98
Leu Leu Gly Leu Met Met Val Val Thr Gly Asp Glu Asp Glu Asn Ser
-10 -5 1 5
ccg tgt gcc cat gag gcc ctc ctg gac gag gac acc ctc ttt tgc cag 146
Pro Cys Ala His Glu Ala Leu Leu Asp Glu Asp Thr Leu Phe Cys Gln
10 15 20
ggc ctt gaa gtt ttc tac cca gag ttg ggg aac att ggc tgc aag gtt 194
Gly Leu Glu Val Phe Tyr Pro Glu Leu Gly Asn Ile Gly Cys Lys Val
25 30 35
gtt cct gat tgt aac aac tac aga cag aag atc acc tcc tgg atg gag 242
Val Pro Asp Cys Asn Asn Tyr Arg Gln Lys Ile Thr Ser Trp Met Glu
40 45 50
ccg ata gtc aag ttc ccg ggg gcc gtg gac ggc gca acc tat atc ctg 290
Pro Ile Val Lys Phe Pro Gly Ala Val Asp Gly Ala Thr Tyr Ile Leu
55 60 65 70
gtg atg gtg gat cca gat gcc cct agc aga gca gaa ccc aga cag aga 338
Val Met Val Asp Pro Asp Ala Pro Ser Arg Ala Glu Pro Arg Gln Arg
75 80 85
ttc tgg aga cat tgg ctg gta aca gat atc aag ggc gcc gac ctg aag 386
Phe Trp Arg His Trp Leu Val Thr Asp Ile Lys Gly Ala Asp Leu Lys
90 95 100
aaa ggg aag att cag ggc cag gag tta tca gcc tac cag gct ccc tcc 434
Lys Gly Lys Ile Gln Gly Gln Glu Leu Ser Ala Tyr Gln Ala Pro Ser
105 110 115
cca ccg gca cac agt ggc ttc cat cgc tac cag ttc ttt gtc tat ctt 482
Pro Pro Ala His Ser Gly Phe His Arg Tyr Gln Phe Phe Val Tyr Leu
120 125 130
cag gaa gga aag gtc atc tct ctc ctt ccc aag gaa aac aaa act cga 530
Gln Glu Gly Lys Val Ile Ser Leu Leu Pro Lys Glu Asn Lys Thr Arg
135 140 145 150
ggc tct tgg aaa atg gac aga ttt ctg aac cgt ttc cac ctg ggc gaa 578
Gly Ser Trp Lys Met Asp Arg Phe Leu Asn Arg Phe His Leu Gly Glu
155 160 165
cct gaa gca agc acc cag ttc atg acc cag aac tac cag gac tca cca 626
Pro Glu Ala Ser Thr Gln Phe Met Thr Gln Asn Tyr Gln Asp Ser Pro
170 175 180
acc ctc cag gct ccc aga gaa agg gcc agc gag ccc aag cac aaa aac 674
Thr Leu Gln Ala Pro Arg Glu Arg Ala Ser Glu Pro Lys His Lys Asn
185 190 195
cag gcg gag ata gct gcc tgc tagatagccg gctttgccat ccgggcatgt 725
Gln Ala Glu Ile Ala Ala Cys
200 205
ggccacactg cccaccaccg acgatgtggg tatggaaccc cctctggata cagaacccct 785
tcttttccaa ataaaaaaaa aatcatccaa aaaaaaaaaa a 826

<210> 125
<211> 571
<212> DNA
<213> Homo sapiens

<220>
<221> CDS

<222> 74..295

<221> sig_peptide
<222> 74..196
<223> Von Heijne matrix
score 5.4
seq RLLYIGFLGYCSG/LI

<221> polyA_signal
<222> 545..550

<221> polyA_site
<222> 561..571

<400> 125
cgggtagtgg tcgtcgtggt tttccttgta gttcgtggtc tgagaccagg cctcaagtgg 60
aaacggcgtc acc atg atc gca cgg cgg aac cca gta ccc tta cgg ttt 109
Met Ile Ala Arg Arg Asn Pro Val Pro Leu Arg Phe
-40 -35 -30
ctg ccg gat gag gcc cgg agc ctg ccc ccg ccc aag ctg acc gac ccg 157
Leu Pro Asp Glu Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro
-25 -20 -15
cgg ctc ctc tac atc ggc ttc ttg ggc tac tgc tcc ggc ctg att gat 205
Arg Leu Leu Tyr Ile Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp
-10 -5 1
aac ctg atc cgg cgg agg ccg atc gcg acg gct ggt ttg cat cgc cag 253
Asn Leu Ile Arg Arg Arg Pro Ile Ala Thr Ala Gly Leu His Arg Gln
5 10 15
ctt cta tat att acg gcc ttt ttt ttg ctg gat att atc ttg 295
Leu Leu Tyr Ile Thr Ala Phe Phe Leu Leu Asp Ile Ile Leu
20 25 30
taaaacgtga agactacctg tatgctgtga gggaccgtga aatgtttgga tatatgaaat 355
tacatccaga ggattttcct gaagaagata agaaaacata tggtgaaatt tttgaaaaat 415
tccatccaat acgttgaagt cttcaaaatg cttgctccag tttcactgat acctgctgtt 475
cctgaatttg atggaacatg tttcttatga cagttgaagc ttatgctaat ctgtatgttg 535
acaccttgta attaaaatac gtaccaaaaa aaaaaa 571

<210> 126
<211> 659
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 440..658

<221> polyA_signal
<222> 601..606

<400> 126
cgccttacga gctgggaggt ggtgcctctc acccagctaa ttgctctcta gcccttggcc 60
ttcacaggtg ttggtgcctg ccgtgaacgc attctgacct gggccgtatc tgtctcccaa 120
gactttgtgc ctatggttgg ggacagagtg aggtcgttgc cttgacgacg acagcatgcg 180
gcccgtggtc ctcctaagtg tgagcttgcg gcggaccgag gcccacctgc ctccctgcct 240
gcttcgccca ggactcgtga ctgcgtccgc agaagaaatc acaacagcgc tggaattgct 300
agtttgctag gcagcatctt ttggacctgc gaaccatatg catttcacct caaatctgtt 360
tccaagttga aaacctttgg gtctttctat gcgaacggat tgaagaaacg caaaaagttt 420
ctacggactt taaattaaa atg gaa aaa tat gaa aac ctg ggt ttg gtt gga 472
Met Glu Lys Tyr Glu Asn Leu Gly Leu Val Gly
1 5 10

```
gaa ggg agt tat gga atg gtg atg aag tgt agg aat aaa gat act gga        520
Glu Gly Ser Tyr Gly Met Val Met Lys Cys Arg Asn Lys Asp Thr Gly
            15                  20                  25
aga att gtg gcc ata aag aag ttc tta gaa agt gac gat gac aaa atg        568
Arg Ile Val Ala Ile Lys Lys Phe Leu Glu Ser Asp Asp Asp Lys Met
        30                  35                  40
gtt aaa aag att gca atg cga gaa gtc aag tta cta aag caa ctt agg        616
Val Lys Lys Ile Ala Met Arg Glu Val Lys Leu Leu Lys Gln Leu Arg
    45                  50                  55
cat gaa aac ttg gtg aat ctc ttg gaa gtg tgt aaa aaa aaa a              659
His Glu Asn Leu Val Asn Leu Leu Glu Val Cys Lys Lys Lys
60                  65                  70


<210> 127
<211> 301
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 38..283

<221> sig_peptide
<222> 38..85
<223> Von Heijne matrix
      score 4.1
      seq LLPATSLAGPVLS/TL

<221> polyA_signal
<222> 257..262

<400> 127
cacctgaatc ccaggaaccc tcaatgaggt cttcaag atg aag aga ctg ctg cca        55
                                         Met Lys Arg Leu Leu Pro
                                                 -15
gct acc agc ctg gct ggc cct gtc ctg tcc acc ctc att gcc cca act        103
Ala Thr Ser Leu Ala Gly Pro Val Leu Ser Thr Leu Ile Ala Pro Thr
-10                 -5                  1               5
ccc atg ttg ttt tgt gaa gat aaa agc tgg gat ctt ttt ctt ttt ttt        151
Pro Met Leu Phe Cys Glu Asp Lys Ser Trp Asp Leu Phe Leu Phe Phe
            10                  15                  20
aag tct cac aag aca tgg ggc atc tcc aca aat tta agt tcc tgt cca        199
Lys Ser His Lys Thr Trp Gly Ile Ser Thr Asn Leu Ser Ser Cys Pro
        25                  30                  35
ttt gga aat ttg ttt cta tgt gta cag ttt gtc aga gaa aaa caa agt        247
Phe Gly Asn Leu Phe Leu Cys Val Gln Phe Val Arg Glu Lys Gln Ser
    40                  45                  50
ttt tgt atg aat aca gaa tgt gat tta cgc aag aat tgacaaaaaa             293
Phe Cys Met Asn Thr Glu Cys Asp Leu Arg Lys Asn
55                  60                  65
aaaaaaaa                                                               301


<210> 128
<211> 477
<212> DNA
<213> Homo sapiens

<220>
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<221> CDS
<222> 121..477

<221> sig_peptide
<222> 121..288
<223> Von Heijne matrix
score 3.5
seq SSCADSFVSSSSS/QP

<400> 128
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cctcggagca ggcggagtaa agggacttga gcgagccagt tgccggatta ttctatttcc       60
cctccctctc tcccgccccg tatctctttt caccccttctc ccaccctcgc tcgcgtagcc     120
atg gcg gag ccg tcg gcg gcc act cag tcc cat tcc atc tcc tcg tcg        168
Met Ala Glu Pro Ser Ala Ala Thr Gln Ser His Ser Ile Ser Ser Ser
    -55                 -50                 -45
tcc ttc gga gcc gag ccg tcc gcg ccc ggc ggc ggc ggg agc cca gga        216
Ser Phe Gly Ala Glu Pro Ser Ala Pro Gly Gly Gly Gly Ser Pro Gly
-40                 -35                 -30                 -25
gcc tgc ccc gcc ctg ggg acg aag agc tgc agc tcc tcc tgt gcg gat        264
Ala Cys Pro Ala Leu Gly Thr Lys Ser Cys Ser Ser Ser Cys Ala Asp
                -20                 -15                 -10
tcc ttt gtt tct tcc tct tcc tct cag cct gta tct cta ttt tcg acc        312
Ser Phe Val Ser Ser Ser Ser Ser Gln Pro Val Ser Leu Phe Ser Thr
             -5                   1               5
tca caa gag gga ttg agc tct ctt tgc tct gat gag cca tct tca gaa        360
Ser Gln Glu Gly Leu Ser Ser Leu Cys Ser Asp Glu Pro Ser Ser Glu
    10                  15                  20
att atg act tct tcc ttt ctt tca tct tct gaa ata cat aac act ggc        408
Ile Met Thr Ser Ser Phe Leu Ser Ser Ser Glu Ile His Asn Thr Gly
25                  30                  35                  40
ctt aca ata cta cat gga gaa aaa agc cat gtg tta ggg agc cag cct        456
Leu Thr Ile Leu His Gly Glu Lys Ser His Val Leu Gly Ser Gln Pro
                45                  50                  55
att tta gcc aaa aaa aaa aaa                                            477
Ile Leu Ala Lys Lys Lys Lys
            60
```

<210> 129
<211> 323
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..163

<221> polyA_signal
<222> 292..297

<221> polyA_site
<222> 310..323

<400> 129
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a gct ttc gtg tgg gag cca gct atg gtg cgg atc aat gcg ctg aca gca       49
  Ala Phe Val Trp Glu Pro Ala Met Val Arg Ile Asn Ala Leu Thr Ala
  1               5                   10                  15
gcc tct gag gct gcg tgc ctg atc gtg tct gta gat gaa acc atc aag         97
Ala Ser Glu Ala Ala Cys Leu Ile Val Ser Val Asp Glu Thr Ile Lys
            20                  25                  30
aac ccc cgc tcg act gtg gat gct ccc aca gca gca ggc cgg ggc cgt        145
```

```
Asn Pro Arg Ser Thr Val Asp Ala Pro Thr Ala Ala Gly Arg Gly Arg
        35                  40                  45
ggt cgt ggc cgc ccc cac tgagaggcac cccacccatc acatggctgg        193
Gly Arg Gly Arg Pro His
    50
ctggctgctg ggtgcactta ccctccttgg cttggttact tcattttaca aggaaggggt    253
agtaattggc ccactctctt cttactggag gctatttaaa taaaatgtaa gacttcaaaa    313
aaaaaaaaaa                                                           323
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<210> 130
<211> 1392
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..675

<221> sig_peptide
<222> 46..87
<223> Von Heijne matrix
score 5.3
seq LTLLGLSFILAGL/IV

<221> polyA_signal
<222> 1364..1369

<221> polyA_site
<222> 1383..1392

<400> 130

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ctccgagttg ccacccagga aaaagagggc tcctctggga gatgt atg ctt act ctc     57
                                                  Met Leu Thr Leu
tta ggc ctt tca ttc atc ttg gca gga ctt att gtt ggt gga gcc tgc     105
Leu Gly Leu Ser Phe Ile Leu Ala Gly Leu Ile Val Gly Gly Ala Cys
-10                 -5                  1               5
att tac aag tac ttc atg ccc aag agc acc att tac cgt gga gag atg     153
Ile Tyr Lys Tyr Phe Met Pro Lys Ser Thr Ile Tyr Arg Gly Glu Met
            10                  15                  20
tgc ttt ttt gat tct gag gat cct gca aat tcc ctt cgt gga gga gag     201
Cys Phe Phe Asp Ser Glu Asp Pro Ala Asn Ser Leu Arg Gly Gly Glu
        25                  30                  35
cct aac ttc ctg cct gtg act gag gag gct gac att cgt gag gat gac     249
Pro Asn Phe Leu Pro Val Thr Glu Glu Ala Asp Ile Arg Glu Asp Asp
    40                  45                  50
aac att gca atc att gat gtg cct gtc ccc agt ttc tct gat agt gac     297
Asn Ile Ala Ile Ile Asp Val Pro Val Pro Ser Phe Ser Asp Ser Asp
55                  60                  65                  70
cct gca gca att att cat gac ttt gaa aag gga atg act gct tac ctg     345
Pro Ala Ala Ile Ile His Asp Phe Glu Lys Gly Met Thr Ala Tyr Leu
                75                  80                  85
gac ttg ttg ctg ggg atc tgc tat ctg atg ccc ctc aat act tct att     393
Asp Leu Leu Leu Gly Ile Cys Tyr Leu Met Pro Leu Asn Thr Ser Ile
            90                  95                  100
gtt atg cct cca aaa aat ctg gta gag ctc ttt ggc aaa ctg gcg agt     441
Val Met Pro Pro Lys Asn Leu Val Glu Leu Phe Gly Lys Leu Ala Ser
        105                 110                 115
ggc aga tat ctg cct caa act tat gtg gtt cga gaa gac cta gtt gct     489
Gly Arg Tyr Leu Pro Gln Thr Tyr Val Val Arg Glu Asp Leu Val Ala
    120                 125                 130
```

```
gtg gag gaa att cgt gat gtt agt aac ctt ggc atc ttt att tac caa      537
Val Glu Glu Ile Arg Asp Val Ser Asn Leu Gly Ile Phe Ile Tyr Gln
135                 140                 145                 150
ctt tgc aat aac aga aag tcc ttc cgc ctt cgt cgc aga gac ctc ttg      585
Leu Cys Asn Asn Arg Lys Ser Phe Arg Leu Arg Arg Arg Asp Leu Leu
                155                 160                 165
ctg ggt ttc aac aaa cgt gcc att gat aaa tgc tgg aag att aga cac      633
Leu Gly Phe Asn Lys Arg Ala Ile Asp Lys Cys Trp Lys Ile Arg His
            170                 175                 180
ttc ccc aac gaa ttt att gtt gag acc aag atc tgt caa gag              675
Phe Pro Asn Glu Phe Ile Val Glu Thr Lys Ile Cys Gln Glu
        185                 190                 195
taagaggcaa cagatagagt gtccttggta ataagaagtc agagatttac aatatgactt    735
taacattaag gtttatggga tactcaagat atttactcat gcatttactc tattgcttat    795
gctttaaaaa aaggaaaaaa aaaaaactac taaccactgc aagctcttgt caaattttag    855
tttaattggc attgcttgtt ttttgaaact gaaattacat gagtttcatt ttttctttgc    915
atttataggg tttagatttc tgaaagcagc atgaatatat cacctaacat cctgacaata    975
aattccatcc gttgtttttt ttgtttgttt gtttttcttt ttcctttaag taagctcttt   1035
attcatctta tggtggagca attttaaaat ttgaaatatt ttaaattgtt tttgaacttt   1095
ttgtgtaaaa tatatcagat ctcaacattg ttggtttctt ttgtttttca ttttgtacaa   1155
ctttcttgaa tttagaaatt acatctttgc agttctgtta ggtgctctgt aattaacctg   1215
acttatatgt gaacaatttt catgagacag tcatttttaa ctaatgcagt gattctttct   1275
cactactatc tgtattgtgg aatgcacaaa attgtgtagg tgctgaatgc tgtaaggagt   1335
ttaggttgta tgaattctac aaccctataa taaattttac tctatacaaa aaaaaaa      1392


<210> 131
<211> 999
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 62..385

<221> polyA_signal
<222> 974..979

<221> polyA_site
<222> 987..999

<400> 131
cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct     60
g atg gga tgt gtt ttc cag agc aca gaa gac aaa tgt ata ttc aag ata    109
  Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Cys Ile Phe Lys Ile
  1               5                   10                  15
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta      157
Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu
            20                  25                  30
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc      205
Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg
        35                  40                  45
gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc      253
Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu
    50                  55                  60
caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc      301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg
65                  70                  75                  80
ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg      349
Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val
                85                  90                  95
```

```
ctt cca gag gag ccc aaa ggt acg caa atg ctt act taaagagggg           395
Leu Pro Glu Glu Pro Lys Gly Thr Gln Met Leu Thr
        100                 105
ccaaggggca agagctttca tgtgcaagag gcaaggaaac tgattatctt gagtaaatgc    455
cagcctttgg gctaagtact taccacagag tgaatcttca aaaaatgatc ataattattt    515
cagtcaataa aaatagagtt attttattaa ataaaatatt gataattatt gtattattac    575
tttaaacaca cttccccctc acaaaagccc tgtgaaggat gttttgttca catatatgtc    635
caaatatgtt ttggacacat atttattaaa tggaataaat agtacttgaa ccctggcacc    695
tctgacaaca aagtccatgt tctttttact atgccctaat acctttcatc agttatccac    755
attgatgcta catctgtatt ttataggtac cctatgttag gtgttctggg ggatagaaaa    815
gaaataagca ggccaggctc agtggctcat gcctgtaatc ctagcatttt gggaggctga    875
ggcagcagaa ctgcctgagc cccagggttc aagactgcag tgagctatga tggcaccact    935
gcattctagc ctgggtgaca gagcaagact ctgtctaaaa taaaaaaaga gaaaaaaaaa    995
aaaa                                                                  999
```

```
&lt;210&gt; 132
&lt;211&gt; 725
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; CDS
&lt;222&gt; 422..550

&lt;221&gt; sig_peptide
&lt;222&gt; 422..475
&lt;223&gt; Von Heijne matrix
      score 4.5
      seq LRWLMPVIPALWG/AE

&lt;221&gt; polyA_site
&lt;222&gt; 714..725

&lt;400&gt; 132
tctgcgaggg tgggagagaa aattaggggg agaaaggaca gagagagcaa ctaccatcca     60
tagccagata ggtgagtaaa tatatttgca gtaacctatt tgctattcct tgctgcaact    120
gtgtttaatg ttccttccag aatcagagag agtattgcca tccaagaaat cgtttttaga    180
tatgacattt gagctatcat cttgagacca atacctaaaa caatttcagt ttaagaaatg    240
tctaggtatg gtgaaaacac agtttaaaac cagcaaaaca gaatttattg ccctcagcga    300
atacccacaa tgtacatata ccttgtattt ctgaaagcaa agcaagcatg ccaagtagtt    360
tttatttacc tgtacctata atacagcaag gtgaaacagg atatattttt gaagtttaaa    420
a atg tct tca ggc cgg ctg cgg tgg ctc atg cct gta atc cca gca ctt    469
  Met Ser Ser Gly Arg Leu Arg Trp Leu Met Pro Val Ile Pro Ala Leu
          -15                 -10                 -5
tgg gga gcc gag aag ggt gaa tca cct gag gtc agc agt ttt gag acc      517
Trp Gly Ala Glu Lys Gly Glu Ser Pro Glu Val Ser Ser Phe Glu Thr
        1               5                   10
agg ctg gcc aac atg gcg aaa ccc tgt ctc tac tgaaaataca aaaattagct    570
Arg Leu Ala Asn Met Ala Lys Pro Cys Leu Tyr
15                  20                  25
gggtgtggtg gcgggcgcct gtagtcccag ctacttggga gactgaggca ggagaattgc    630
ttgaacacgg aaggcggaag ttgcagtaag ctgagatcgt gccaccgcac accagcttgg    690
gcaacagagt gagactccct ctcaaaaaaa aaaaa                               725
```

```
&lt;210&gt; 133
&lt;211&gt; 400
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens
```

<220>
<221> CDS
<222> 124..231

<221> polyA_site
<222> 387..400

<400> 133
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ctcgcctctc ctggcttctg gtatgcacca gcaattcctg gcgttccttg gctcctagaa      60
gcatcactcc tatcacatgg tcatcttcac cctgtgtgtc ttcacactac cctttctctg     120
tgc atg tct gcc cga atc cct ttt tat aag gac acc agt cag att aga       168
    Met Ser Ala Arg Ile Pro Phe Tyr Lys Asp Thr Ser Gln Ile Arg
    1               5                   10                  15
tta ggg tct acc ata ata cct cat ttt aac tta atc acc ttt gta aag       216
Leu Gly Ser Thr Ile Ile Pro His Phe Asn Leu Ile Thr Phe Val Lys
                20                  25                  30
acc ttt ttc caa ata tagtcactct ctgaggtact gatggttagg atctcaacat      271
Thr Phe Phe Gln Ile
            35
accttttttg ggaggacaca attgaaccca taacagggtg tttgcaagga agagttaaaa     331
tttgaaagaa aggtggtatt tgcttagata gatagggcac agctttctag gtgacaaaaa     391
aaaaaaaaa                                                             400
```

<210> 134
<211> 1053
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 131..1051

<221> sig_peptide
<222> 131..169
<223> Von Heijne matrix
score 4.2
seq MLAVSLTVPLLGA/MM

<221> polyA_signal
<222> 1019..1024

<400> 134
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gagcgaggcg gacgggctgc gacagcgccg gcccctgcgg ccgcaggtcg tcacagacga      60
tgatggccag gccccggagg ctaaggacgg cagctccttt agcggcagag ttttccgagt     120
gaccttcttg atg ctg gct gtt tct ctc acc gtt ccc ctg ctt gga gcc        169
           Met Leu Ala Val Ser Leu Thr Val Pro Leu Leu Gly Ala
                       -10                 -5
atg atg ctg ctg gaa tct cct ata gat cca cag cct ctc agc ttc aaa       217
Met Met Leu Leu Glu Ser Pro Ile Asp Pro Gln Pro Leu Ser Phe Lys
1               5                   10                  15
gaa ccc ccg ctc ttg ctt ggt gtt ctg cat cca aat acg aag ctg cga       265
Glu Pro Pro Leu Leu Leu Gly Val Leu His Pro Asn Thr Lys Leu Arg
                20                  25                  30
cag gca gaa agg ctg ttt gaa aat caa ctt gtt gga ccg gag tcc ata       313
Gln Ala Glu Arg Leu Phe Glu Asn Gln Leu Val Gly Pro Glu Ser Ile
            35                  40                  45
gca cat att ggg gat gtg atg ttt act ggg aca gca gat ggc cgg gtc       361
Ala His Ile Gly Asp Val Met Phe Thr Gly Thr Ala Asp Gly Arg Val
    50                  55                  60
```

```
gta aaa ctt gaa aat ggt gaa ata gag acc att gcc cgg ttt ggt tcg       409
Val Lys Leu Glu Asn Gly Glu Ile Glu Thr Ile Ala Arg Phe Gly Ser
65                  70                  75                  80
ggc cct tgc aaa acc cga gat gat gag cct gtg tgt ggg aga ccc ctg       457
Gly Pro Cys Lys Thr Arg Asp Asp Glu Pro Val Cys Gly Arg Pro Leu
                85                  90                  95
ggt atc cgt gca ggg ccc aat ggg act ctc ttt gtg gcc gat gca tgc       505
Gly Ile Arg Ala Gly Pro Asn Gly Thr Leu Phe Val Ala Asp Ala Cys
            100                 105                 110
aag gga cta ttt gaa gta aat ccc tgg aaa cgt gaa gtg aaa ctg ctg       553
Lys Gly Leu Phe Glu Val Asn Pro Trp Lys Arg Glu Val Lys Leu Leu
        115                 120                 125
ctg tcc tcc gag aca ccc att gag ggg aag aac atg tcc ttt gtg aat       601
Leu Ser Ser Glu Thr Pro Ile Glu Gly Lys Asn Met Ser Phe Val Asn
    130                 135                 140
gat ctt aca gtc tct cag gat ggg agg aag att tat ttc acc gat tct       649
Asp Leu Thr Val Ser Gln Asp Gly Arg Lys Ile Tyr Phe Thr Asp Ser
145                 150                 155                 160
agc agc aaa tgg caa aga cga gac tac ctg ctt ctg gtg atg gag ggc       697
Ser Ser Lys Trp Gln Arg Arg Asp Tyr Leu Leu Leu Val Met Glu Gly
                165                 170                 175
aca gat gac ggg cgc ctg ctg gag tat gat act gtg acc agg gaa gta       745
Thr Asp Asp Gly Arg Leu Leu Glu Tyr Asp Thr Val Thr Arg Glu Val
            180                 185                 190
aaa gtt tta ttg gac cag ctg cgg ttc ccg aat gga gtc cag ctg tct       793
Lys Val Leu Leu Asp Gln Leu Arg Phe Pro Asn Gly Val Gln Leu Ser
        195                 200                 205
cct gca gaa gac ttt gtc ctg gtg gca gaa aca acc atg gcc agg ata       841
Pro Ala Glu Asp Phe Val Leu Val Ala Glu Thr Thr Met Ala Arg Ile
    210                 215                 220
cga aga gtc tac gtt tct ggc ctg atg aag ggc ggg gct gat ctg ttt       889
Arg Arg Val Tyr Val Ser Gly Leu Met Lys Gly Gly Ala Asp Leu Phe
225                 230                 235                 240
gtg gag aac atg cct gga ttt cca gac aac atc cgg ccc agc agc tct       937
Val Glu Asn Met Pro Gly Phe Pro Asp Asn Ile Arg Pro Ser Ser Ser
                245                 250                 255
ggg ggg tac tgg gtg ggc atg tcg acc atc cgc cct aac cct ggg ttt       985
Gly Gly Tyr Trp Val Gly Met Ser Thr Ile Arg Pro Asn Pro Gly Phe
            260                 265                 270
tcc atg ctg gat ttc tta tct gag aga ccc tgg att aaa agg atg att      1033
Ser Met Leu Asp Phe Leu Ser Glu Arg Pro Trp Ile Lys Arg Met Ile
        275                 280                 285
ttt aag gca aaa aaa aaa aa                                           1053
Phe Lys Ala Lys Lys Lys
    290
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<210> 135
<211> 1128
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 86..403

<221> sig_peptide
<222> 86..181
<223> Von Heijne matrix
score 8.8
seq VPMLLLIVGGSFG/LR

<221> polyA_signal
<222> 1097..1102

<221> polyA_site
<222> 1117..1128

<400> 135
cgtcttggtg agagcgtgag ctgctgagat ttgggagtct gcgctaggcc cgcttggagt 60
tctgagccga tggaagagtt cactc atg ttt gca ccc gcg gtg atg cgt gct 112
Met Phe Ala Pro Ala Val Met Arg Ala
-30 -25
ttt cgc aag aac aag act ctc ggc tat gga gtc ccc atg ttg ttg ctg 160
Phe Arg Lys Asn Lys Thr Leu Gly Tyr Gly Val Pro Met Leu Leu Leu
-20 -15 -10
att gtt gga ggt tct ttt ggt ctt cgt gag ttt tct caa atc cga tat 208
Ile Val Gly Gly Ser Phe Gly Leu Arg Glu Phe Ser Gln Ile Arg Tyr
-5 1 5
gat gct gtg aag agt aaa atg gat cct gag ctt gaa aaa aaa ctg aaa 256
Asp Ala Val Lys Ser Lys Met Asp Pro Glu Leu Glu Lys Lys Leu Lys
10 15 20 25
gag aat aaa ata tct tta gag tcg gaa tat gag aaa atc aaa gac tcc 304
Glu Asn Lys Ile Ser Leu Glu Ser Glu Tyr Glu Lys Ile Lys Asp Ser
30 35 40
aag ttt gat gac tgg aag aat att cga gga ccc agg cct tgg gaa gat 352
Lys Phe Asp Asp Trp Lys Asn Ile Arg Gly Pro Arg Pro Trp Glu Asp
45 50 55
cct gac ctc ctc caa gga aga aat cca gaa agc ctt aag act aag aca 400
Pro Asp Leu Leu Gln Gly Arg Asn Pro Glu Ser Leu Lys Thr Lys Thr
60 65 70
act tgactctgct gattcttttt tccnnntttt ttttttttta aataaaaata 453
Thr
ctattaactg gacttcctaa tatatacttc tatcaagtgg aaaggaaatt ccaggcccat 513
ggaaacttgg atatgggtaa tttgatgaca aataatcttc actaaaggtc atgtacaggt 573
ttttatactt cccagctatt ccatctgtgg atgaaagtaa caatgttggc cacgtatatt 633
ttacacctcg aaataaaaaa tgtgaatact gctccaaaaa aaaaaaccag taccgtgtag 693
tctctctcgt ggcttggatt tacactgggc aacgtggttg gaatgtatct ggctcagaac 753
tatgatatac caaacctggc taaaaaactt gaagaaatta aaaaggactt ggatgccaag 813
aagaaacccc ctagtgcatg agactgcctc cagcactgcc ttcaggatat accgattcta 873
ctgctcttga gggcctcgtt tactatctga accaaaagct tttgttttcg tctccagcct 933
cagcacttct cttctttgct agaccctgtg ttttttgctt taaagcaagc aaaatggggc 993
cccaatttga gaactacccg acgtttccaa catactcacc tcttcccata atccctttcc 1053
aactgcatgg gaggttctaa gactggaatt atggtgctag attagtaaac atgactttta 1113
acgaaaaaaa aaaaa 1128

<210> 136
<211> 254
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 37..162

<221> sig_peptide
<222> 37..93
<223> Von Heijne matrix
score 9.5
seq LMCLSLCTAFALS/KP

<221> polyA_signal
<222> 224..229

<221> polyA_site
<222> 243..254

<400> 136
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tgtgctgtgg gggctacgag gaaagatcta attatc atg gac ctg cga cag ttt      54
                                        Met Asp Leu Arg Gln Phe
                                                        -15
ctt atg tgc ctg tcc ctg tgc aca gcc ttt gcc ttg agc aaa ccc aca     102
Leu Met Cys Leu Ser Leu Cys Thr Ala Phe Ala Leu Ser Lys Pro Thr
            -10                 -5                  1
gaa aag aag gac cgt gta cat cat gag cct cag ctc agt gac aag gtt     150
Glu Lys Lys Asp Arg Val His His Glu Pro Gln Leu Ser Asp Lys Val
    5                   10                  15
cac aat gat att tgatagaacc aattgttgta cataaaacag atctgcgcat         202
His Asn Asp Ile
20
atatatatat gtataaaaaa taataaaata atggaagatg aaaaaaaaaa aa           254
```

<210> 137
<211> 886
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 31..381

<221> sig_peptide
<222> 31..90
<223> Von Heijne matrix
score 5.4
seq AFVIACVLSLIST/IY

<221> polyA_site
<222> 875..886

<400> 137
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ggaggatggg cgagcagtct gaatggcaga atg gat aac cgt ttt gct aca gca      54
                                 Met Asp Asn Arg Phe Ala Thr Ala
                                 -20                 -15
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca     102
Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala
        -10                 -5                  1
gcc tcc att ggc aca gac ttc tgg tat gaa tat cga agt cca gtt caa     150
Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln
5                   10                  15                  20
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt     198
Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser
                25                  30                  35
gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat     246
Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn
            40                  45                  50
ggc aca gtg gga ttg tgg gga cgg tgt atc acc ata ccc aaa aac atg     294
Gly Thr Val Gly Leu Trp Gly Arg Cys Ile Thr Ile Pro Lys Asn Met
        55                  60                  65
cat tgg tat agc cca cca gaa agg aca ggt att tct ctt att tta act     342
His Trp Tyr Ser Pro Pro Glu Arg Thr Gly Ile Ser Leu Ile Leu Thr
```

```
   70                   75                   80
tct gtc ttc ttc acc tgg tta ata ata gac aaa acg acg taatgattgc       391
Ser Val Phe Phe Thr Trp Leu Ile Ile Asp Lys Thr Thr
85                  90                   95
ccaattacat gtaagcaggt ttgttggttc tctctctcct taaagaaata aatcgtgtat    451
cttctctttc tactgccttc tctccccaac ttctttgcat taccatggta ctcatcaata    511
ttggttggat gaggaacttt tcttatcttg ggaaagcctt aatggctttt tttttctta     571
tttactcact cattaaaata cttttcatta ctctaacaca tgttataaag aaatagttgg    631
aaaagtgcat cgaaagactt ttaaaaatat ttggtaacta gtaaaaggac taccatcgaa    691
aatcaactca aaaaattgtc cttttatggg ttagctgtat tataatacat atctatcatt    751
tgcccctgtg tcttagagga tataatttga ccagctctac atttaatctg tgtaattatg    811
agactgtttt acaacaatct tgatgcagag ttggtaggtt aagaaatttg tattacagaa    871
gttaaaaaaa aaaaa                                                      886
```

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<210> 138
<211> 1244
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..579

<221> sig_peptide
<222> 46..156
<223> Von Heijne matrix
      score 3.5
      seq LVFNFLLILTILT/IW

<400> 138
ccttatcca ggttnttatc tanggaatcc cnnnaagact gggga atg gag aga cag      57
                                                 Met Glu Arg Gln
                                                             -35
tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna      105
Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa
            -30                 -25                 -20
gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg      153
Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu
        -15                 -10                 -5
aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act      201
Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr
    1               5                   10                  15
gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat      249
Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr
                20                  25                  30
gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta      297
Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val
            35                  40                  45
aaa cta act ttc agt cca cca act ctg ctg gtt aat gtc act gac caa      345
Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn Val Thr Asp Gln
        50                  55                  60
gtt tat gaa tat aaa tac aaa aga gaa ata agt cag cac aac atc aat      393
Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln His Asn Ile Asn
    65                  70                  75
cct cat caa gga aat gct ata ctt gaa aag atg aca ttt gat cca gaa      441
Pro His Gln Gly Asn Ala Ile Leu Glu Lys Met Thr Phe Asp Pro Glu
80                  85                  90                  95
atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat      489
Ile Phe Phe Asn Val Leu Leu Pro Pro Ile Ile Phe His Ala Gly Tyr
                100                 105                 110
```

```
agt cta aag aag aga cac ttt ttt caa aac tta gga tct att tta acg      537
Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly Ser Ile Leu Thr
            115                 120                 125
tat gcc ttc ttg gga act gcc atc tcc tgc atc gtc ata ggg              579
Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val Ile Gly
        130                 135                 140
taagtgacat tcggagctca agttgcaggt ggctgtgggg tctgtgatct gtgtgaggga    639
tctaacactt ccaggattct tgctggctgg gaaaattgtc tttttttag tatatcacat     699
atttgtatgt tttttctgac ttaattccac ggcttctgac aaatacaagg cttcaaatca    759
aagcaaacta gaggattgct ggactttctc tgtgagttct ggacttctga cttagggaat    819
gtggatcact tgccttgagt tatgtgaagc gcattgcatt cttcttttag tttgagtaat    879
gccgatatgg tcactgcatt ctttttgtc ttgtattgag agaccttacc tgtatttggc     939
aggagtgcaa aagtaactat atgccaagag ttttctttct aaaggaaagt ttacaagaca    999
gcagtctgaa acagatatgn tccaaatatn naacagagtt gcttaataca gggatagctt   1059
ttcagttaat accctgtaga atgcagactc tttntttcat tgtattttct tgattatgct   1119
actgagccct aagtcacacg ttatatactc tggcttgcag ctcatcataa agtaaaatgt   1179
ggtaccaaat ggtgaaggca atccagcctn tgataatccc gtccaataca ttaaagntcc   1239
actgc                                                                1244
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<210> 139
<211> 471
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 92..469

<221> sig_peptide
<222> 92..172
<223> Von Heijne matrix
      score 7.9
      seq VVVLALGFLGCYG/AK

<221> polyA_signal
<222> 454..459

<221> polyA_site
<222> 458..471

<400> 139
gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcctttct      60
gaagatcttc gggccactgt cgtccagtgc c atg cag ttt gtc aac gtg ggc         112
                                  Met Gln Phe Val Asn Val Gly
                                              -25
tac ttc ctc atc gca gcc ggc gtt gtg gtc ctt gct ctt ggt ttc ctg      160
Tyr Phe Leu Ile Ala Ala Gly Val Val Val Leu Ala Leu Gly Phe Leu
-20                 -15                 -10                 -5
ggc tgc tat ggt gct aag act gag agc atg tgt gcc ctc gtg acg ttc      208
Gly Cys Tyr Gly Ala Lys Thr Glu Ser Met Cys Ala Leu Val Thr Phe
                1               5                   10
ttc ttc atc ctc ctc ctc atc ttc att gct gag gtt gca gct gct gtg      256
Phe Phe Ile Leu Leu Leu Ile Phe Ile Ala Glu Val Ala Ala Ala Val
        15                  20                  25
gtc gcc ctg gtg tac acc aca atg gct gag cac ttc ctg acg ttg ctg      304
Val Ala Leu Val Tyr Thr Thr Met Ala Glu His Phe Leu Thr Leu Leu
    30                  35                  40
gta gtg cct gcc atc aag aaa gat tat ggt tcc cag gaa gac ttc act      352
Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp Phe Thr
45                  50                  55                  60
```

```
caa gtg tgg aac acc acc atg aaa ggg ctc aag tgc cgt ggc ttc acc      400
Gln Val Trp Asn Thr Thr Met Lys Gly Leu Lys Cys Arg Gly Phe Thr
                65                  70                  75
aac tat acg gat ttt gag gac tca ccc tac ttc aaa atg cat aaa cct      448
Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Met His Lys Pro
            80                  85                  90
gtt aca atg aaa aaa aaa aaa aa                                       471
Val Thr Met Lys Lys Lys Lys
        95
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<210> 140
<211> 849
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 154..675

<221> sig_peptide
<222> 154..498
<223> Von Heijne matrix
score 4.8
seq PLRLLNLLILIEG/GV

<221> polyA_signal
<222> 819..824

<221> polyA_site
<222> 838..849

<400> 140

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cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac      60
agaatcaagg aggttctctt caactccctc ttcagtgcct actatgttgc atttctcccc      120
ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac      174
                                     Met Arg Trp Ser Cys Glu His
                                         -115                -110
ctc gtt atg gtg tgg atc aat gct ttt gtc atg ctc acc acg caa ctg      222
Leu Val Met Val Trp Ile Asn Ala Phe Val Met Leu Thr Thr Gln Leu
            -105                -100                -95
ttg cca tcc aaa tac tgt gat ttg cta cat aaa tca gct gct cac ctg      270
Leu Pro Ser Lys Tyr Cys Asp Leu Leu His Lys Ser Ala Ala His Leu
        -90                 -85                 -80
ggc aag tgg cag aag ttg gaa cat ggg tcc tac agc aat gct cca cag      318
Gly Lys Trp Gln Lys Leu Glu His Gly Ser Tyr Ser Asn Ala Pro Gln
    -75                 -70                 -65
cac att tgg tca gaa aat aca ata tgg cct caa ggg gtg ctg gtg cgg      366
His Ile Trp Ser Glu Asn Thr Ile Trp Pro Gln Gly Val Leu Val Arg
-60                 -55                 -50                 -45
cac agc aga tgt tta tat aga gcc atg ggg cct tac aac gtg gca gtg      414
His Ser Arg Cys Leu Tyr Arg Ala Met Gly Pro Tyr Asn Val Ala Val
                -40                 -35                 -30
cct tca gat gta tct cat gcc cgc ttt tat ttc tta ttt cat cga cca      462
Pro Ser Asp Val Ser His Ala Arg Phe Tyr Phe Leu Phe His Arg Pro
            -25                 -20                 -15
tta agg ctg tta aat ctg ctc atc ctt att gag ggc ggt gtc gtc ttc      510
Leu Arg Leu Leu Asn Leu Leu Ile Leu Ile Glu Gly Gly Val Val Phe
        -10                 -5                  1
tat cag ctc tat tcc ttg ctg cgg tcg gag aag tgg aac cac aca ctt      558
Tyr Gln Leu Tyr Ser Leu Leu Arg Ser Glu Lys Trp Asn His Thr Leu
```

```
5                   10                  15                  20
tcc atg gct ctc atc ctc ttc tgc aac tac tat gtt tta ttt aaa ctt     606
Ser Met Ala Leu Ile Leu Phe Cys Asn Tyr Tyr Val Leu Phe Lys Leu
                25                  30                  35
ctc cgg gac aga ata gta tta ggc agg gca tac tcc tac cca ctc aac     654
Leu Arg Asp Arg Ile Val Leu Gly Arg Ala Tyr Ser Tyr Pro Leu Asn
            40                  45                  50
agt tat gaa ctc aag gca aac taagctgcct ctcaacaatg agggagaact        705
Ser Tyr Glu Leu Lys Ala Asn
        55
cagataaaaa tattttcata cgttctattt ttttcttgtg atttttataa atatttaaga   765
tgttttatat tttgtatact attatgtttt gaaagtcggg aagagtaagg gatattaaat   825
gtatccgtaa acaaaaaaaa aaaa                                          849
```

```
<210> 141
<211> 155
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -31..-1

<400> 141
Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser
    -30                 -25                 -20
Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu
-15                 -10                 -5                  1
Leu Leu Pro His Cys Gln Lys Pro Phe Val Tyr Asp Leu His Ala Val
            5                   10                  15
Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys
        20                  25                  30
Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe
    35                  40                  45
Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu
50                  55                  60                  65
Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu
                70                  75                  80
Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser
            85                  90                  95
Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu Phe Leu
        100                 105                 110
Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile
    115                 120
```

```
<210> 142
<211> 55
<212> PRT
<213> Homo sapiens

<400> 142
Met Ala Asp Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg
1               5                   10                  15
Met Tyr Tyr Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe
            20                  25                  30
Phe Met Gly Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln
        35                  40                  45
Lys Gln Lys Lys Arg Ser Asn
```

50 55

<210> 143
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 143
Met Ser Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser
-20 -15 -10 -5
Leu Ile Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg
1 5 10
Leu Glu Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val
15 20 25
Gln Glu Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe
30 35 40
Gly Arg Lys
45

<210> 144
<211> 198
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 144
Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr
-20 -15 -10
Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His
-5 1 5 10
Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala
15 20 25
Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Trp Leu Thr Lys Ala Arg
30 35 40
Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu
45 50 55
Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu
60 65 70 75
Glu Thr Gln Met Glu Glu Asp Ile Leu Gln Leu Gln Ala Glu Ala Thr
80 85 90
Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp
95 100 105
Ser Val Gln Arg Leu Glu Val Gln Leu Arg Ser Ala Trp Leu Gly Pro
110 115 120
Ala Tyr Arg Glu Phe Glu Val Leu Lys Ala His Ala Asp Lys Gln Ser
125 130 135
His Ile Leu Trp Ala Leu Thr Gly His Val Gln Arg Gln Arg Arg Glu
140 145 150 155
Met Val Ala Gln Gln His Arg Leu Arg Gln Ile Gln Glu Arg Leu His
160 165 170
Thr Ala Ala Leu Pro Ala

175

<210> 145
<211> 135
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -25..-1

<400> 145
Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu Val Val Met
-25 -20 -15 -10
Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg Ile Lys Ser
-5 1 5
Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro Glu Gln Asp
10 15 20
Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln Gly Lys Xaa
25 30 35
Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn Leu Ser Phe
40 45 50 55
Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Ile Arg Lys Asn Trp
60 65 70
Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu Gly Thr Tyr
75 80 85
Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln Ser Gln Ser
90 95 100
Lys Gln Lys Ser Ile Glu Glu
105 110

<210> 146
<211> 255
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -70..-1

<400> 146
Met Gln Gln Lys Glu Gln Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe
-70 -65 -60 -55
Pro Gln Ile Arg Trp Lys Ile Gln Glu Ser Ile Glu Arg Leu Arg Val
-50 -45 -40
Ile Ala Asn Glu Ile Glu Lys Val His Arg Gly Cys Val Ile Ala Asn
-35 -30 -25
Val Val Ser Gly Ser Thr Gly Ile Leu Ser Val Ile Gly Val Met Leu
-20 -15 -10
Ala Pro Phe Thr Ala Gly Leu Ser Leu Ser Ile Thr Ala Ala Gly Val
-5 1 5 10
Gly Leu Gly Ile Ala Ser Ala Thr Ala Gly Ile Ala Ser Ser Ile Val
15 20 25
Glu Asn Thr Tyr Thr Arg Ser Ala Glu Leu Thr Ala Ser Arg Leu Thr
30 35 40
Ala Thr Ser Thr Asp Gln Leu Glu Ala Leu Arg Asp Ile Leu His Asp
45 50 55
Ile Thr Pro Asn Val Leu Ser Phe Ala Leu Asp Phe Asp Glu Ala Thr

```
    60                  65                  70
Lys Met Ile Ala Asn Asp Val His Thr Leu Arg Arg Ser Lys Ala Thr
75                  80                  85                  90
Val Gly Arg Pro Leu Ile Ala Trp Arg Tyr Val Pro Ile Asn Val Val
                95                  100                 105
Glu Thr Leu Arg Thr Arg Gly Ala Pro Thr Arg Ile Val Arg Lys Val
            110                 115                 120
Ala Arg Asn Leu Gly Lys Ala Thr Ser Gly Val Leu Val Val Leu Asp
        125                 130                 135
Val Val Asn Leu Val Gln Asp Ser Leu Asp Leu His Lys Gly Glu Lys
    140                 145                 150
Ser Glu Ser Ala Glu Leu Leu Arg Gln Trp Ala Gln Glu Leu Glu Glu
155                 160                 165                 170
Asn Leu Asn Glu Leu Thr His Ile His Gln Ser Leu Lys Ala Gly
                175                 180                 185
```

<210> 147
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -49..-1

<400> 147

```
Met Pro Gly Thr Glu Val Leu Glu Gly Ala Thr Asp Gly Leu Ala Ala
                -45                 -40                 -35
Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu Gly Gly Ser Val Ile Ser
            -30                 -25                 -20
Met Ile Val Leu Leu Ile Cys Val Val Cys Leu Tyr Ile Val Cys Arg
        -15                 -10                 -5
Cys Gly Ser His Leu Trp Arg Glu Ser His His
    1                   5                   10
```

<210> 148
<211> 180
<212> PRT
<213> Homo sapiens

<400> 148

```
Met Cys Ile Ser Gly Leu Cys Gln Ile Val Gly Cys Asp His Gln Leu
1               5                   10                  15
Gly Ser Thr Val Lys Glu Asp Asn Cys Gly Val Cys Asn Gly Asp Gly
            20                  25                  30
Ser Thr Cys Arg Leu Val Arg Gly Gln Tyr Lys Ser Gln Leu Ser Ala
        35                  40                  45
Thr Lys Ser Asp Asp Thr Val Val Ala Ile Pro Tyr Gly Ser Arg His
    50                  55                  60
Ile Arg Leu Val Leu Lys Gly Pro Asp His Leu Tyr Leu Glu Thr Lys
65                  70                  75                  80
Thr Leu Gln Gly Thr Lys Gly Glu Asn Ser Leu Ser Ser Thr Gly Thr
                85                  90                  95
Phe Leu Val Asp Asn Ser Ser Val Asp Phe Gln Lys Phe Pro Asp Lys
            100                 105                 110
Glu Ile Leu Arg Met Ala Gly Pro Leu Thr Ala Asp Phe Ile Val Lys
        115                 120                 125
Ile Arg Asn Ser Gly Ser Ala Asp Ser Thr Val Gln Phe Ile Phe Tyr
```

```
    130                          135                          140
Gln Pro Ile Ile His Arg Trp Arg Glu Thr Asp Phe Phe Pro Cys Ser
145                     150                     155                 160
Ala Thr Cys Gly Gly Gly Tyr Gln Leu Thr Ser Ala Glu Cys Tyr Asp
                165                     170                     175

Leu Arg Ser Asn
            180
```

<210> 149
<211> 162
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -23..-1

<400> 149
```
Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala
            -20                 -15                 -10
Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
        -5                  1               5
Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
10                  15                  20                  25
Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val
                30                  35                  40
Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu
            45                  50                  55
Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr
        60                  65                  70
Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe
    75                  80                  85
Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Pro Asp Asn
90                  95                  100                 105
Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr
                110                 115                 120
Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Val Ser Met
            125                 130                 135

Val Phe
```

<210> 150
<211> 120
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -23..-1

<400> 150
```
Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala
            -20                 -15                 -10
Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
        -5                  1               5
Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
10                  15                  20                  25
Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val
                30                  35                  40
```

```
Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu
            45                  50                  55
Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr
        60                  65                  70
Cys Ile Arg Ser Lys Asn Gly Pro Gly Thr Ala Val His Ala Tyr Asn
    75                  80                  85
Pro Ser Thr Phe Arg Gly Gln Val
90                  95
```

<210> 151
<211> 7
<212> PRT
<213> Homo sapiens

<400> 151

```
Met Val Glu Met Thr Gly Val
1               5
```

<210> 152
<211> 199
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -42..-1

<400> 152

```
Met Asp Gly Gln Lys Lys Asn Trp Lys Asp Lys Val Val Asp Leu Leu
        -40                 -35                 -30
Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu
    -25                 -20                 -15
Phe Leu Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala
-10                 -5                  1                   5
Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr
            10                  15                  20
Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe
        25                  30                  35
Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln
    40                  45                  50
Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu
55                  60                  65                  70
Leu Arg Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe
                75                  80                  85
Ala Val Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly
            90                  95                  100
Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val
        105                 110                 115
Ile Tyr Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Val Leu Ala
    120                 125                 130
Asn Lys Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro
135                 140                 145                 150
Gly Leu Lys Arg Lys Ala Glu
                155
```

<210> 153

<211> 43
<212> PRT
<213> Homo sapiens

<400> 153
Met Pro Phe Arg Met Ser Gly Tyr Ile Pro Phe Gly Thr Pro Ile Val
1 5 10 15
Ser Val Thr Phe Lys Gly Phe Pro Phe Leu Lys Asn Tyr Phe Lys Cys
20 25 30
Leu Thr Leu Cys Tyr Cys Ser Arg Val Phe Asp
35 40

<210> 154
<211> 50
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -37..-1

<400> 154
Met Glu Trp Ala Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro
-35 -30 -25
Gly Trp Asp His Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe
-20 -15 -10
Ser Gly Ser Gln Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala
-5 1 5 10
Gln Glu

<210> 155
<211> 153
<212> PRT
<213> Homo sapiens

<400> 155
Thr Val Pro Leu Leu Leu Glu Pro Ala Asp His Ala Arg Gly Arg Ala
1 5 10 15
His Val His Leu Pro Glu Asn Val Arg Ser Gln Ser Pro Gly His Val
20 25 30
Arg Arg Gly Arg Ser Gly Ala Gln Val Leu Pro Thr Gly Pro Asp Glu
35 40 45
Lys Gln Val Glu Lys Ser Glu Val Asp Phe Ser Lys Ser His Ser Leu
50 55 60
Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Lys Thr
65 70 75 80
Gly Ser Gln Val Phe Arg Ser Glu Asn Trp Lys Val Trp Ala Glu Ser
85 90 95
Ser Arg Gly Asp His Asp Asp Cys Leu Asp Leu Cys Ser Val Leu Cys
100 105 110
Trp Gly Glu Leu Leu Arg Thr Ile Pro Glu Ile Pro Pro Lys Arg Gly
115 120 125
Glu Leu Lys Thr Glu Leu Leu Gly Leu Lys Glu Arg Lys His Lys Pro
130 135 140
Gln Val Ser Gln Gln Glu Glu Leu Lys
145 150

<210> 156
<211> 67
<212> PRT
<213> Homo sapiens

<400> 156
Met Arg Gln Lys Arg Lys Gly Asp Leu Ser Pro Ala Lys Leu Met Met
1   5   10   15
Leu Thr Ile Gly Asp Val Ile Lys Gln Leu Ile Glu Ala His Glu Gln
            20   25   30
Gly Lys Asp Ile Asp Leu Asn Lys Val Arg Thr Lys Thr Ala Ala Lys
        35   40   45
Tyr Gly Leu Ser Ala Gln Pro Arg Leu Val Asp Ile Ile Ala Ala Val
    50   55   60
Pro Pro Glu
65

<210> 157
<211> 87
<212> PRT
<213> Homo sapiens

<400> 157
Met Asp Glu Leu Ser Glu Glu Asp Lys Leu Thr Val Ser Arg Ala Arg
1   5   10   15
Lys Ile Gln Arg Phe Leu Ser Gln Pro Phe Gln Val Ala Glu Val Phe
            20   25   30
Thr Gly His Met Gly Lys Leu Val Pro Leu Lys Glu Thr Ile Lys Gly
        35   40   45
Phe Gln Gln Ile Leu Ala Gly Glu Tyr Asp His Leu Pro Glu Gln Ala
    50   55   60
Phe Tyr Met Val Gly Pro Ile Glu Glu Ala Val Ala Lys Ala Asp Lys
65   70   75   80
Leu Ala Glu Glu His Ser Ser
                85

<210> 158
<211> 250
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -85..-1

<400> 158
Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe Leu
-85   -80   -75   -70
Leu Leu Ala Lys Ser Ala Lys Gly Ala Ala Leu Ala Thr Leu Ile His
                -65   -60   -55
Gln Val Leu Glu Ala Pro Gly Val Tyr Val Phe Gly Glu Leu Leu Asp
            -50   -45   -40
Met Pro Asn Val Arg Glu Leu Xaa Ala Arg Asn Leu Pro Pro Leu Thr
        -35   -30   -25
Glu Ala Gln Lys Asn Lys Leu Arg His Leu Ser Val Val Thr Leu Ala
    -20   -15   -10
Ala Lys Val Lys Cys Ile Pro Tyr Ala Val Leu Leu Glu Ala Leu Ala

```
-5                  1                   5                        10
Leu Arg Asn Val Arg Gln Leu Glu Asp Leu Val Ile Glu Ala Val Tyr
            15                  20                       25
Ala Asp Val Leu Arg Gly Ser Leu Asp Gln Arg Asn Gln Arg Leu Glu
        30                  35                       40
Val Asp Tyr Ser Ile Gly Arg Asp Ile Gln Arg Gln Asp Leu Ser Ala
    45                  50                       55
Ile Ala Arg Thr Leu Gln Glu Trp Cys Val Gly Cys Glu Val Val Leu
60                  65                       70                   75
Ser Gly Ile Glu Glu Gln Val Ser Arg Ala Asn Gln His Lys Glu Gln
                80                  85                       90
Gln Leu Gly Leu Lys Gln Gln Ile Glu Ser Glu Val Ala Asn Leu Lys
            95                  100                      105
Lys Thr Ile Lys Val Thr Thr Ala Ala Ala Ala Ala Ala Thr Ser Gln
        110                 115                      120
Asp Pro Glu Gln His Leu Thr Glu Leu Arg Glu Pro Ala Pro Gly Thr
    125                 130                      135
Asn Gln Arg Gln Pro Ser Lys Lys Ala Ser Lys Gly Lys Gly Leu Arg
140                 145                      150                  155
Gly Ser Ala Lys Ile Trp Ser Lys Ser Asn
                160                 165
```

<210> 159
<211> 24
<212> PRT
<213> Homo sapiens

<400> 159

```
Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys
1               5                   10                  15
His Ile Asn Ile Ser Phe His Arg
            20
```

<210> 160
<211> 228
<212> PRT
<213> Homo sapiens

<400> 160

```
Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys
1               5                   10                  15
His Ile Asn Ile Ser Phe His Arg Phe Pro Leu Asp Pro Lys Arg Arg
            20                  25                  30
Lys Glu Trp Val Arg Leu Val Arg Arg Lys Asn Phe Val Pro Gly Lys
        35                  40                  45
His Thr Phe Leu Cys Ser Lys His Phe Glu Ala Ser Cys Phe Asp Leu
    50                  55                  60
Thr Gly Gln Thr Arg Arg Leu Lys Met Asp Ala Val Pro Thr Ile Phe
65                  70                  75                  80
Asp Phe Cys Thr His Ile Lys Ser Met Lys Leu Lys Ser Arg Asn Leu
                85                  90                  95
Leu Lys Lys Asn Asn Ser Cys Ser Pro Ala Gly Pro Ser Ser Leu Lys
            100                 105                 110
Ser Asn Ile Ser Ser Gln Gln Val Leu Leu Glu His Ser Tyr Ala Phe
        115                 120                 125
Arg Asn Pro Met Glu Ala Lys Lys Arg Ile Ile Lys Leu Glu Lys Glu
    130                 135                 140
Ile Ala Ser Leu Arg Arg Lys Met Lys Thr Cys Leu Gln Lys Glu Arg
```

```
145                     150                     155                     160
Arg Ala Thr Arg Arg Trp Ile Lys Ala Met Cys Leu Val Lys Asn Leu
                165                     170                     175
Glu Ala Asn Ser Val Leu Pro Lys Gly Thr Ser Glu His Met Leu Pro
            180                     185                     190
Thr Ala Leu Ser Ser Leu Pro Leu Glu Asp Phe Lys Ile Leu Glu Gln
        195                     200                     205
Asp Gln Gln Asp Lys Thr Leu Leu Ser Leu Asn Leu Lys Gln Thr Lys
    210                     215                     220
Ser Thr Phe Ile
225
```

```
<210> 161
<211> 86
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 161
Met Asn Leu His Phe Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly
-20                 -15                 -10                  -5
Leu Val Leu Ala Pro Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe
                1               5                   10
Pro Cys Ile Tyr Cys Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala
        15                  20                  25
Phe Ser Phe Ile Thr Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu
    30                  35                  40
Ile Leu Pro Glu Lys Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly
45                  50                  55                  60
Pro Ala Lys Leu Arg Gln
                65
```

```
<210> 162
<211> 44
<212> PRT
<213> Homo sapiens

<400> 162
Met Ser Pro Arg Leu Glu Cys Ser Gly Ala Ile Leu Ala His Cys Asn
1               5                   10                  15
Pro Arg Leu Pro Gly Ser Ser Tyr Ser Pro Ala Ser Ala Thr Trp Val
            20                  25                  30
Arg Gly Ser Leu Glu Pro Gly Arg Leu Arg Leu Gln
        35                  40
```

```
<210> 163
<211> 314
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -58..-1
```

<400> 163
Met Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala
-55 -50 -45
Glu Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly
-40 -35 -30
Val Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His
-25 -20 -15
His Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys
-10 -5 1 5
Ala Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro
10 15 20
Cys Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala
25 30 35
Ile Ile Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His
40 45 50
Asn Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu
55 60 65 70
Glu Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu
75 80 85
Glu Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr
90 95 100
Glu Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg
105 110 115
Lys Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp
120 125 130
Ala Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys
135 140 145 150
Tyr Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg
155 160 165
Gln Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His
170 175 180
Val Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro
185 190 195
Pro Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys
200 205 210
Ile Ile Glu Thr Val Ala Glu Gly Gly Gly Glu Leu Gly Val His Met
215 220 225 230
Tyr Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile
235 240 245
Glu Tyr Asp Tyr Thr Arg His Phe Thr Met
250 255

<210> 164
<211> 89
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -80..-1

<400> 164
Met Arg Thr Arg Thr Thr Gly Asn Pro Arg Gly Leu His Asp Thr Phe
-80 -75 -70 -65
Pro Arg Arg Pro Arg Leu Gly Arg Cys Ser Asp Met Asp Thr Ala Arg
-60 -55 -50
Thr Ser Cys Ser Asp Leu Leu Pro Trp Glu Gly Val Thr Glu Pro Ala
-45 -40 -35
Leu Cys Gly Asp Gln Leu Gln Gly Thr Glu Gly Trp Leu Glu Ala Thr

```
        -30                 -25                 -20
Gln Leu Gly Arg Gly Leu Leu Ser Ala Cys Ala Pro Trp Gly Asp Gly
    -15                 -10                 -5
Ser Thr Gln Pro Val Pro Leu Cys Ser
1               5
```

<210> 165
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 165

```
Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
-15                 -10                 -5                  1
Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu
            5                   10                  15
Gln Gly Gly Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
        20                  25                  30
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
    35                  40                  45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Val Phe
50                  55                  60                  65
Arg Arg Glu Leu Ser Glu Tyr Thr Glu Gly Leu Thr Ser Glu Pro Leu
                70                  75                  80
Thr Ala
```

<210> 166
<211> 92
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -36..-1

<400> 166

```
Met Leu Val Thr Gln Gly Leu Val Tyr Gln Gly Tyr Leu Ala Ala Asn
    -35                 -30                 -25
Ser Arg Phe Gly Ser Leu Pro Lys Val Ala Leu Ala Gly Leu Leu Gly
-20                 -15                 -10                 -5
Phe Gly Leu Gly Lys Val Ser Tyr Ile Gly Val Cys Gln Ser Lys Phe
                1               5                   10
His Phe Phe Glu Asp Gln Leu Arg Gly Ala Gly Phe Gly Pro Gln His
        15                  20                  25
Asn Arg His Cys Leu Leu Thr Cys Glu Glu Cys Lys Ile Lys His Gly
    30                  35                  40
Leu Ser Glu Lys Gly Asp Ser Gln Pro Ser Ala Ser
45                  50                  55
```

<210> 167
<211> 351
<212> PRT

<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 167
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Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys Ser Gly
    -15                 -10                 -5
Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr
1               5                   10                  15
Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile
            20                  25                  30
Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr
        35                  40                  45
Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu
    50                  55                  60
Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro Glu Pro
65                  70                  75                  80
Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser
                85                  90                  95
Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu
            100                 105                 110
Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu
        115                 120                 125
Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr
    130                 135                 140
Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met
145                 150                 155                 160
Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr
                165                 170                 175
Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser
            180                 185                 190
Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu
        195                 200                 205
Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile
    210                 215                 220
Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser
225                 230                 235                 240
Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp
                245                 250                 255
Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser
            260                 265                 270
Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val
        275                 280                 285
Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys
    290                 295                 300
His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Cys
305                 310                 315                 320
His Leu Gly His Gly Arg Leu Trp Leu Gln His Ser Thr Asp Arg
                325                 330                 335
```

<210> 168
<211> 138
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -47..-1

<400> 168
Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu
-45 -40 -35
Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser
-30 -25 -20
Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile
-15 -10 -5 1
Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu
5 10 15
Ala Gly Leu Cys Thr Leu Gly Ser Val Ser Cys Tyr Val Ala Gly Ile
20 25 30
Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp Asn Val Ser Gly Glu
35 40 45
Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser Ala Pro Leu Gln Phe
50 55 60 65
Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His Thr Asn Arg Arg Glu
70 75 80
Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala
85 90

<210> 169
<211> 101
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -73..-1

<400> 169
Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu Cys Arg
-70 -65 -60
Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp Leu Val
-55 -50 -45
Asn Ile Phe Trp Phe Tyr Arg Glu Ala Phe Leu Val Pro Ala Tyr Thr
-40 -35 -30
Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val Gly Phe
-25 -20 -15 -10
Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe Gln Ile
-5 1 5
Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe Thr Ile
10 15 20
Pro Leu Gly Thr Pro
25

<210> 170
<211> 252
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -68..-1

<400> 170
Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu
-65 -60 -55

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                 Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg
                     -25                 -20                 -15
cct ctc gct tct ttg cag tgg agc ctg aca ctg gcg tgg tgt ggc tcc      278
Pro Leu Ala Ser Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser
                -10                  -5                   1
ggc agc cac tgg aca gag aga cca akt cag akt tca ccg tgg akt tct      326
Gly Ser His Trp Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser
          5                  10                  15
ctg tca gcg acc acc agg ggg tgatcacacg gaaggtgaac atccaggtcg         377
Leu Ser Ala Thr Thr Arg Gly
     20                  25
gggatgtgaa tgacaacgcg cccacatttc acaatcagcc ctacagcgtc cgcatccctg    437
araatacacc agtggggacg cccatcttca tcgtgaatgc cacagacccc gacttggggg    497
caggggggcag cgtcctctac tccttccagc ccccctccca attcttcgcc attgacagcg   557
cccgcggtat cktcacagtg atccgggagc tggactacga taccacrcmg gcctaccagc    617
tcwcggtcwa cgccacagat caagacaara ccaggcctct gtccaccstg gccaacttgg    677
ccatcatcat cacagatgtc caggacatgg accccatctt catcaacctg ccttacagca    737
ccaacatcta cgagcattct cctccgggca cgacggtgcg catcatcacc gccatagacc    797
aggataaagg acgtccccgg ggcattggct acaccatcgt ttcagggcat ctgtgtttac    857
aagaacccaa gatctctcag gagctcagga aaggggcctt gctgtgaggc tcagggttcc    917
catggacatt ctgagctgac cctcctcagc attggatctc ctggctcagg aactaggaac    977
gaagcttgga tgttttctcc tttcctacag catctgtatt catttcctat agttgccata   1037
ataaaatgcc actaacttag tggcttaaaa accaaaaaaa aaaaaccctt              1087
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<210> 311
<211> 916
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 90..815

<221> sig_peptide
<222> 90..179
<223> Von Heijne matrix
score 13.1999998092651
seq LLLLSTLVIPSAA/AP

<221> polyA_signal
<222> 883..888

<221> polyA_site
<222> 905..916

<400> 311

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aaaacagtac gtgggcggcc ggaatccggg agtccggtga cccgggctgt ggtctagcat     60
aaaggcggag ccagaagaag gggcggggt atg gga gaa gcc tcc cca cct gcc      113
                                Met Gly Glu Ala Ser Pro Pro Ala
                                -30                 -25
ccc gca agg cgg cat ctg ctg gtc ctg ctg ctg ctc ctc tct acc ctg      161
Pro Ala Arg Arg His Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu
        -20                 -15                 -10
gtg atc ccc tcc gct gca gct cct atc cat gat gct gac gcc caa gag      209
Val Ile Pro Ser Ala Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu
     -5                   1               5                  10
agc tcc ttg ggt ctc aca ggc ctc cag agc cta ctc caa ggc ttc agc      257
Ser Ser Leu Gly Leu Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser
                 15                  20                  25
cga ctt ttc ctg aaa ggt aac ctg ctt cgg ggc ata gac agc tta ttc      305
```

```
Arg Leu Phe Leu Lys Gly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe
            30                  35                  40
tct gcc ccc atg gac ttc cgg ggc ctc cct ggg aac tac cac aaa gag     353
Ser Ala Pro Met Asp Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu
        45                  50                  55
gag aac cag gag cac cag ctg ggg aac aac acc ctc tcc agc cac ctc     401
Glu Asn Gln Glu His Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu
    60                  65                  70
cag atc gac aag atg acc gac aac aag aca gga gag gtg ctg atc tcc     449
Gln Ile Asp Lys Met Thr Asp Asn Lys Thr Gly Glu Val Leu Ile Ser
75                  80                  85                  90
gag aat gtg gtg gca tcc att caa cca vcg gag ggg anc ttc gag ggt     497
Glu Asn Val Val Ala Ser Ile Gln Pro Xaa Glu Gly Xaa Phe Glu Gly
                95                  100                 105
gat ttg aag gth ccc agg atg gag gar aag gag gcc ctg gta ccc mtc     545
Asp Leu Lys Val Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Xaa
            110                 115                 120
car aag gcc acg gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc     593
Gln Lys Ala Thr Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala
        125                 130                 135
ttc tgg atc att aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg     641
Phe Trp Ile Ile Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu
    140                 145                 150
gag ggc ggc cac tgg ctc anc gar aag cga cac cgc ctg cag gcc atc     689
Glu Gly Gly His Trp Leu Xaa Glu Lys Arg His Arg Leu Gln Ala Ile
155                 160                 165                 170
cgg gat gga ctc cgc aag ggg acc cac aag gac rtc cta daa rag ggg     737
Arg Asp Gly Leu Arg Lys Gly Thr His Lys Asp Xaa Leu Xaa Xaa Gly
                175                 180                 185
acc gar agc tcc tcc cac tcc agg ctg tcc ccc cga aar amm cac tta     785
Thr Glu Ser Ser Ser His Ser Arg Leu Ser Pro Arg Lys Xaa His Leu
            190                 195                 200
ctg tac atc ctc arg ccc tct cgg cag ctg targggtggg gaccggggar       835
Leu Tyr Ile Leu Xaa Pro Ser Arg Gln Leu
        205                 210
macctgcctg tagcccccat caraccctgc cccaagcacc atatggaaat aaagttcttt   895
cttacatcca aaaaaaaaaa a                                             916
```

<210> 312
<211> 583
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 52..513

<221> sig_peptide
<222> 52..231
<223> Von Heijne matrix
score 4
seq LVRRTLLVAALRA/WM

<221> polyA_signal
<222> 553..558

<221> polyA_site
<222> 572..583

<400> 312

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aaggaaacag caaccagagg gagatgatca cctgaaccac tgctccaaac c atg ggc      57
                                                         Met Gly
                                                         -60
agt aaa tgc tgt aaa ggt ggt cca gat gaa gat gca gta gaa aga cag      105
Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu Arg Gln
            -55                 -50                 -45
agg cgg cag aag ttg ctt ctt gca caa ctg cat cac aga aaa agg gtg      153
Arg Arg Gln Lys Leu Leu Leu Ala Gln Leu His His Arg Lys Arg Val
        -40                 -35                 -30
aar gca gct ggg cag atc cag gcc tgg tgg cgt ggg gtc ctg gtg cgc      201
Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu Val Arg
    -25                 -20                 -15
agg acc ctg ctg gtt gct gcc ctc agg gcc tgg atg att cag tgc tgg      249
Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln Cys Trp
-10                 -5                  1               5
tgg agg acg ttg gtg cag aga cgg atc cgt cag cgg cgg cag gcc ctg      297
Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln Ala Leu
            10                  15                  20
ttr ggg gtc tac gtc atc cag gag cag gcg gcg gtc aag ctc cag tcc      345
Leu Gly Val Tyr Val Ile Gln Glu Gln Ala Ala Val Lys Leu Gln Ser
        25                  30                  35
tgc atc cgc atg tgg cag tgc cgg caa tgt tac cgc caa atg tgc aat      393
Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met Cys Asn
    40                  45                  50
gct ctc tgc ttg ttc cag gtc cca aaa agc agc ctt gcc ttc caa act      441
Ala Leu Cys Leu Phe Gln Val Pro Lys Ser Ser Leu Ala Phe Gln Thr
55                  60                  65                  70
gat ggc ttt tta cag gtc caa tat gca atc cct tca aag cag cca gag      489
Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu
                75                  80                  85
ttc cac att gaa atc cta tca atc tgaaaggcct ggggcatgga gaacaggctg      543
Phe His Ile Glu Ile Leu Ser Ile
            90
cactacccta ataaatgtct gaccaggtaa aaaaaaaaa                           583
```

<210> 313
<211> 697
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 172..438

<221> sig_peptide
<222> 172..354
<223> Von Heijne matrix
score 4.69999980926514
seq LLPCNLHCSWLHS/SP

<221> polyA_signal
<222> 682..687

<221> polyA_site
<222> 685..697

<400> 313

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agattggctg ggcagatggg ctgactggct gggcagatgg gtgggtgagt tccctctccc      60
cagagccatc ggccaggtac caaagctcag ctgtatggat tcccaacagg aggacctgcg     120
cttccctggg acccattgtt gtactggatt aacaagcgac ggcgctacgg c atg aat      177
```

```
                                                              Met Asn
                                                                  -60
gca gcc atc aac acg ggc cct gcc cct gct gtc acc aag act gag act       225
Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr Glu Thr
                -55                 -50                 -45
gag gtc cag aat cca gat gtt ctg tgg gat ttg gac atc ccc gaa gcc       273
Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro Glu Ala
            -40                 -35                 -30
agg agc cat gct gac caa gac agc aac ccc aag gcg gaa gcc ctg ctc       321
Arg Ser His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala Leu Leu
        -25                 -20                 -15
ccc tgc aac ctg cac tgc agc tgg ctc cac agc agc ccc agg cca gat       369
Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg Pro Asp
    -10                 -5                  1               5
ccc cat tcc cac ttc cca tct ktc agg agg tgc cct ttg ccc cac cct       417
Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro His Pro
                10                  15                  20
tgt gca acc tac ccc ccs kgc tgaaccactc tgtctcctat cctttggcca          468
Cys Ala Thr Tyr Pro Pro Xaa
            25
cctgtcctga aaggaatgtt ctcttccatt ccctcctgaa tctggcccag gaagaccata     528
gcttcaatgy caagcctttt ccttcaaaac tgtagcctcc tctcactgaa ggtgggagct     588
gcaggaatca ggtgcagagt aggaaatgga actaacctca ggaaggtggt attgacagag     648
gtcaggaccc acctggatgt catgctatga aacattaaaa gaaaaaaaa                 697


&lt;210&gt; 314
&lt;211&gt; 803
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; CDS
&lt;222&gt; 148..366

&lt;221&gt; sig_peptide
&lt;222&gt; 148..225
&lt;223&gt; Von Heijne matrix
      score 5.5
      seq LFTLLFLIMLVLK/LD

&lt;221&gt; polyA_signal
&lt;222&gt; 770..775

&lt;221&gt; polyA_site
&lt;222&gt; 792..803

&lt;400&gt; 314
aaatgggggg aaaagggcgg aaaaggacaa ggatccaaac tggcgaattt gctgatcttc      60
gcgtccctct ccgctttccg gccggcagcg ctgccagggt atatttcctt ttttccgatc     120
ctgcaacagc ctctttaaac tgtttaa atg aga atg tcc ttg gct cag aga gta     174
                              Met Arg Met Ser Leu Ala Gln Arg Val
                                      -25                 -20
cta ctc acc tgg ctt ttc aca cta ctc ttc ttg atc atg ttg gtg ttg       222
Leu Leu Thr Trp Leu Phe Thr Leu Leu Phe Leu Ile Met Leu Val Leu
        -15                 -10                 -5
aaa ctg gat gag aaa gca cct tgg aac tgg ttc ctc ata ttc att cca       270
Lys Leu Asp Glu Lys Ala Pro Trp Asn Trp Phe Leu Ile Phe Ile Pro
    1               5                   10                  15
gtc tgg ata ttt gat act atc ctt ctt gtc ctg ctg att gtg aaa atg       318
Val Trp Ile Phe Asp Thr Ile Leu Leu Val Leu Leu Ile Val Lys Met
```

```
                    20                    25                   30
gct ggg cgg tgt aag tct ggc ttt gac ctc gac atg gat cac aca ata      366
Ala Gly Arg Cys Lys Ser Gly Phe Asp Leu Asp Met Asp His Thr Ile
            35                    40                  45
taaaaaaaaa aacctggtac ctcattgcac tgtkacttaa attascсttc tgcctcgcac    426
tctgtgctaa actggaacag tttactacca tgaatctatc ctatgtcttc attcctttat    486
gggccttgct ggctggggct ttaacagaac tcggatataa tgtctttttt gtgaaagact    546
gacttctaag tacatcatct cctttctatt gctgttcaac aagttaccat taaagtgttc    606
tgaatctgtc aagcttcaag aataccagag aactgaggga aaataccaaa tgtagtttta    666
tactacttcc ataaaacagg attggtgaat cacggacttc tagtcaacct acagcttaat    726
tattcagcat ttgagttatt gaaatcctta ttatctctat gtaaataaag tttgttttgg    786
acctcaaaaa aaaaaaa                                                   803
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<210> 315
<211> 823
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 175..336

<221> sig_peptide
<222> 175..276
<223> Von Heijne matrix
      score 3.70000004768372
      seq SVLNVGHLLFSSA/CS

<221> polyA_site
<222> 812..823

<400> 315
aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat     60
caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga    120
ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg      177
                                                            Met

atc cct ctg ata agc cac ctt gcc gag gct gct cct cct acc tca tgg      225
Ile Pro Leu Ile Ser His Leu Ala Glu Ala Ala Pro Pro Thr Ser Trp
            -30                 -25                 -20
agc ctt ata tca agt gtg ctg aat gtg ggc cac ctc ctt ttt tcc tct      273
Ser Leu Ile Ser Ser Val Leu Asn Val Gly His Leu Leu Phe Ser Ser
        -15                 -10                 -5
gct tgc agt gtt tca ctc gag gct ttg agt aca aga aac atc aaa gcg      321
Ala Cys Ser Val Ser Leu Glu Ala Leu Ser Thr Arg Asn Ile Lys Ala
    1               5                   10                  15
atc ata ctt atg aaa taatggcttc agattttcct gtccttgatc ccagctggac      376
Ile Ile Leu Met Lys
                20
tgctcaagaa raaatggccc ttttagaasc tgtgatggac tgtggctttg gaaattggca    436
ggatgtagcc aatcaaatgt gcaccaarac caaggaggag tgtgagaagc actatatgaa    496
gcatttcatc aataacccyc tgtttgcatc trscctgctg aacctgaaac aascagrgga    556
agcaaaaact gctgacacag ccattccatt tcactctaca ratgaccctc cccgacckac    616
ctttgactcc ttgctttctc gggacatggc cgggtacwtg ccmgctcgag cagatttcat    676
tgaggaattt gacaattatg cagaatggga cttgagagac attgattttg ttgaagatga    736
ctcggacatt ttacatgctc tgaagatggc tgtggtagat atctatcatt ccaggttaaa    796
ggagagacaa agacgaaaaa aaaaaaa                                        823


<210> 316
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<211> 823
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 191..553

<221> sig_peptide
<222> 191..304
<223> Von Heijne matrix
      score 5.69999980926514
      seq LAFLSCLAFLVLD/TQ

<221> polyA_signal
<222> 766..771

<221> polyA_site
<222> 804..817

<400> 316
aactctgcag ggcctccaag gccaggcttc agggctggga ctcagtcctg aggcactggg      60
gagccatgag gggctgtggc agggaggggc agggtgtgga aagactcccc tggggccatg     120
gtggagatgt gctgaggtct tctccctgat cgtcttctcc tccctgctga ccgacggcta     180
ccagaackag atg gag tct ccg cag ctc cac tgc att ctc aac agc aac        229
           Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn
                       -35                 -30
agc gtg gcc tgc agc ttt gcc gtg gga gcc ggc ttc ctg gcc ttc ctc       277
Ser Val Ala Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu
-25                 -20                 -15                 -10
agc tgc ctg gcc ttc ctc gtc ctg gac aca cag gag acc cgc att gcc       325
Ser Cys Leu Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala
                -5                   1               5
ggc acc cgc ttc aag aca gcc ttc cag ctc ctg gac ttc atc ctg gct       373
Gly Thr Arg Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala
        10                  15                  20
gtt ctc tgg gca gtt gtc tgg ttc atg ggt ttc tgc ttc ctg gcc aac       421
Val Leu Trp Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn
    25                  30                  35
caa tgg cag cat tcg ccg ccc aaa gar kkc ctc ctg ggg agc agc agt       469
Gln Trp Gln His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser
40                  45                  50                  55
gcc cag gca gcc atc ggc stt cac ctt ctt ctc cat cct tgt ctg gat       517
Ala Gln Ala Ala Ile Gly Xaa His Leu Leu Leu His Pro Cys Leu Asp
                60                  65                  70
att cca rgc cta cct ggc akk cca gga cct ccg aaa tgatgctcca            563
Ile Pro Xaa Leu Pro Gly Xaa Pro Gly Pro Pro Lys
            75                  80
gtcccttacm arcgcttcct ggatgaaggt ggcatggtgs kkaacaccct ccccttgccc     623
tctgccaaca gcctgtgaac atgcccacca ctggccccaa cagcctgagt tatgctagct     683
ctgccctgtc cccctgtctg accgctcmaa agtccccccg gcttgctatg atgcctgaca     743
actaaatatc cttatccaaa tcaataaaga gagaatcctc cctccagaag ggtttctaaa     803
aacaaaaaaa aaaahncctt                                                 823


<210> 317
<211> 1112
<212> DNA
<213> Homo sapiens

<220>
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<221> CDS
<222> 106..603

<221> sig_peptide
<222> 106..216
<223> Von Heijne matrix
score 4.30000019073486
seq LWEKLTLLSPGIA/VT

<221> polyA_site
<222> 1102..1112

<400> 317
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agcgattgcg aatcctccgc tgaggtgatt tggatatccc tagaacgttg agggcacgag    60
tcgggtcctg agaccaggtc ctcagccagc agagccacgt tcctt atg agc acc gtg   117
                                                  Met Ser Thr Val
                                                          -35
ggt tta ttt cat ttt cct aca cca ctg acc cga ata tgc ccg gcg cca     165
Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile Cys Pro Ala Pro
            -30                 -25                 -20
tgg gga ctc cgg ctt tgg gag aag ctg acg ttg tta tcc cca gga ata     213
Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu Ser Pro Gly Ile
        -15                 -10                 -5
gct gtc act ccg gtc cag atg gca ggc aag aag gac tac cct gca ctg     261
Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp Tyr Pro Ala Leu
    1               5                   10                  15
ctt tcc ttg gat gag aat gaa ctc gaa gag cag ttt gtg aaa gga cac     309
Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe Val Lys Gly His
                20                  25                  30
ggt cca ggg ggc cag gca acc aac aaa acc agc aac tgc gtg gtg ctg     357
Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn Cys Val Val Leu
            35                  40                  45
aar mac atc ccc tca ggc atc gtt gta aag tgc cat cag aca aga tca     405
Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His Gln Thr Arg Ser
        50                  55                  60
gtt gat cag aac aga aag cta gct cgg aaa atc cta caa gag aaa gta     453
Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu Gln Glu Lys Val
    65                  70                  75
rat gtt ttc tac aat ggt gaa aac agt cct gtt cac aaa gaa aaa cga     501
Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His Lys Glu Lys Arg
80                  85                  90                  95
gaa gcg gcg aag aaa aaa car gaa agg aaa aaa aga gca aag gaa acc     549
Glu Ala Ala Lys Lys Lys Gln Glu Arg Lys Lys Arg Ala Lys Glu Thr
                100                 105                 110
ctg gaa aaa aag aas ctm ctt aaa raa ctg tgg gag tca agt aaa aag     597
Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu Ser Ser Lys Lys
            115                 120                 125
gtc cac tgagaaaaga attagagatt ccaactgaca gaatctgcca gaagctccca      653
Val His
gggaataatg gtggcgagtt ccatcaccag cattattata gtgcttcaaa agaaatattt   713
ttgatgaact taaaagacaa caaatttatt taaatggtgc actaaactgt agtgaacaga   773
gacatgcacg attcaagaat aaaactcggc cgggcacggt ggacggtgcc tcacatctgt   833
aatcccagca ctttgggagg ccgaggcggg cggatcactt gaggtcagga gtttgagacc   893
agcctggcca acatggtgaa accccgtctc tactaaaaat acaaaaaatt agccaggcat   953
ggtggcgggc acctgtaatc ccagctactc gggaggccga ggcaggagaa ttgcgtgaac  1013
ctgggaggcg gaggttgcag tgagctgaga tcgcgccact gcactcaagc ctgggcaaca  1073
cctgggtgac agagcaagac cccatcycaa aaaaaaaa                         1112
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<210> 318
<211> 1623

<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 47..586

<221> sig_peptide
<222> 47..124
<223> Von Heijne matrix
score 6.30000019073486
seq GVGLVTLLGLAVG/SY

<221> polyA_signal
<222> 1583..1588

<221> polyA_site
<222> 1614..1623

<400> 318
agggatctgt cggcttgtca ggtggtggag gaaaaggcgc tccgtc atg ggg atc 55
Met Gly Ile
-25
cag acg agc ccc gtc ctg ctg gcc tcc ctg ggg gtg ggg ctg gtc act 103
Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly Leu Val Thr
-20 -15 -10
ctg ctc ggc ctg gct gtg ggc tcc tac ttg gtt cgg agg tcc cgc cgg 151
Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg Ser Arg Arg
-5 1 5
cct cag gtc act ctc ctg gac ccc aat gaa aag tac ctg cta cga ctg 199
Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu Leu Arg Leu
10 15 20 25
cta gac aag acg act gtg agc cac aac acc aag agg ttc cgc ttt gcc 247
Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe Arg Phe Ala
30 35 40
ctg ccc acc gcc cac cac act ctg ggg ctg cct gtg ggc aaa cat atc 295
Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly Lys His Ile
45 50 55
tac ctc tcc acm mga att gat ggc agc ctg gtc atc agg cca tac act 343
Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg Pro Tyr Thr
60 65 70
cct gtc acc agt gat gag gat caa ggc tat gtg gat ctt gtc mtc aag 391
Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu Val Xaa Lys
75 80 85
gtc tac ctg aag ggt gtg cac ccc aaa ttt cct gag gga ggg aar atg 439
Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly Gly Lys Met
90 95 100 105
tct cak tac ctg gat asc ctg aaa gtt ggg gat btg gtg gaa ttt csg 487
Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val Glu Phe Xaa
110 115 120
ggg cca agc ggg ttg ctc act tac act gga aaa ggg cat ttt aac att 535
Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His Phe Asn Ile
125 130 135
cag ccc aac aag aat ctc cac cag aac ccc gag tgg cga aga aac tgg 583
Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg Arg Asn Trp
140 145 150
gaa tgattgccgg cgggacagga atcaccccaa tgctacagct gatccgggcc 636
Glu
atcctgaaag tccctgaaga tccaacccag tgctttctgc tttttgccaa ccagacagaa 696
aaggatatca tcttgcggga ggacttagag gaactgcagg cccgctatcc caatcgcttt 756
aagctctggt tcactctgga tcatccccca aaagrttggg cctacagcaa gggctttgtg 816
actgccgacw tgatccggga acacctgccc gctccagggg atgatgtgct ggtactgctt 876

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tgtgggccmc ccccaatggt gcagctggcc tgccatccca acttggacaa actgggctac    936
tcacaaaaga tgcgattcac ctactgagca tcctccagct tccctggtgc tgttcgctgc    996
agttgttccc catcagtact caagcactak aagccttagr ktccctktcct cagagtttca   1056
ggtttttttca gttrsatcka gagctgaaat ctggatagta cctgcaggaa caatattcct   1116
gtagccatgg aagagggcca aggctcagtc actccttgga tggcctccta aatctccccg   1176
tggcaacagg tccaggagag gcccatggag cagtctcttc catggagtaa gaaggaaggg   1236
agcatgtacg cttggtccaa gattggctag ttccttgata gcatcttact ctcaccttct   1296
ttgtgtctgt gatgaaagga acagtctgtg caatgggttt tacttaaact tcactgttca   1356
acctatgagc aaatctgtat gtgtgagtat aagttgagca tagcatactt ccagaggtgg   1416
tcttatggag atggcaagaa aggaggaaat gatttcttca gatctcaaag gagtctgaaa   1476
tatcatattt ctgtgtgtgt cdctctcagc ccctgcccad gctagaggga wacagctact   1536
gataatcgaa aactgctgtt tgtgggcarg aacccctggc tgtgcaaata atggggctga   1596
ngccctgtgt gatattgaaa aaaaaaa                                        1623
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<210> 319
<211> 526
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 99..371

<221> sig_peptide
<222> 99..290
<223> Von Heijne matrix
score 3.79999995231628
seq LFIVVCVICVTLN/FP

<221> polyA_signal
<222> 491..496

<221> polyA_site
<222> 513..524

<400> 319

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attggattag tagaattgct tttgtcattc cattgttttc atatatttgt ttgggacatt     60
ttactttttt ctgttaacgc ttaccctagr aattagaa atg aca cca cgt att ctt    116
                                          Met Thr Pro Arg Ile Leu
                                                              -60

agc gaa gtc cag ttt tca gca ttt tgt cct tat tgg aca ata gca agg      164
Ser Glu Val Gln Phe Ser Ala Phe Cys Pro Tyr Trp Thr Ile Ala Arg
            -55                 -50                 -45

ata tta gaa cgt gtt ggt tcc gcg tgc ttc cgt ctt gag tta tgt gct      212
Ile Leu Glu Arg Val Gly Ser Ala Cys Phe Arg Leu Glu Leu Cys Ala
        -40                 -35                 -30

gct att gtc gga tat ttt gtc tta gat gta cgt act ttc ctg ttc att      260
Ala Ile Val Gly Tyr Phe Val Leu Asp Val Arg Thr Phe Leu Phe Ile
    -25                 -20                 -15

gtg gta tgt gta att tgc gtt act ttg aat ttt cca cgt ttt tac ttt      308
Val Val Cys Val Ile Cys Val Thr Leu Asn Phe Pro Arg Phe Tyr Phe
-10                 -5                  1               5

ctt tgt ctc tca tca ctt acc gct ttt ggg acc ccc ccc atc ggg gtt      356
Leu Cys Leu Ser Ser Leu Thr Ala Phe Gly Thr Pro Pro Ile Gly Val
            10                  15                  20

cac att ccc tct ccc tararcacac tcccttggat ttcctcradt ggggtctgct      411
His Ile Pro Ser Pro
        25

gcggtgaagc tttcccattt tatgtgcaga ttattttcag agggtatata gaattcaggc   471
agctgtttcg ttgtagcaca ttaaaaatat tttcccactt caaaaaaaaa aaacc        526
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<210> 320
<211> 989
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 44..814

<221> sig_peptide
<222> 44..112
<223> Von Heijne matrix
      score 8.30000019073486
      seq VRLLLXLLLLLIA/LE

<221> polyA_site
<222> 978..989

<400> 320
aaatgtgtac acgcccagct tcctgcctgt tactctccac agt atg cga aga ata      55
                                                Met Arg Arg Ile
                                                            -20
tcc ctg act tct agc cct gtg cgc ctt ctt ttg tdt ctg ctg ttg cta     103
Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Leu Xaa Leu Leu Leu Leu
                -15                 -10                 -5
cta ata gcc ttg gag atc atg gtt ggt ggt cac tct ctt tgc ttc aac     151
Leu Ile Ala Leu Glu Ile Met Val Gly Gly His Ser Leu Cys Phe Asn
            1               5                   10
ttc act ata aaa tca ttg tcc aga cct gga cag ccc tgg tgt gaa gcg     199
Phe Thr Ile Lys Ser Leu Ser Arg Pro Gly Gln Pro Trp Cys Glu Ala
    15                  20                  25
cat gtc ttc ttg aat aaa aat ctt ttc ctt cag tac aac agt gac aac     247
His Val Phe Leu Asn Lys Asn Leu Phe Leu Gln Tyr Asn Ser Asp Asn
30                  35                  40                  45
aac atg gtc aaa cct ctg ggc ctc ctg ggg aag aag gta tat gcc acc     295
Asn Met Val Lys Pro Leu Gly Leu Leu Gly Lys Lys Val Tyr Ala Thr
                50                  55                  60
agc act tgg gga gaa ttg acc caa acg ctg gga gaa gtg ggg cga gac     343
Ser Thr Trp Gly Glu Leu Thr Gln Thr Leu Gly Glu Val Gly Arg Asp
            65                  70                  75
ctc agg atg ctc ctt tgt gac atc aaa ccc car ata aag acc agt gat     391
Leu Arg Met Leu Leu Cys Asp Ile Lys Pro Gln Ile Lys Thr Ser Asp
        80                  85                  90
cct tcc act ctg caa gtc kar atk ttt tgt caa cgt gaa gca gaa cgg     439
Pro Ser Thr Leu Gln Val Xaa Xaa Phe Cys Gln Arg Glu Ala Glu Arg
    95                  100                 105
tgc act ggt gca tcc tgg cag ttc gcc acc aat gga gag aaa tcc ctc     487
Cys Thr Gly Ala Ser Trp Gln Phe Ala Thr Asn Gly Glu Lys Ser Leu
110                 115                 120                 125
ctc ttt gac gca atg aac atg acc tgg aca gta att aat cat gaa gcc     535
Leu Phe Asp Ala Met Asn Met Thr Trp Thr Val Ile Asn His Glu Ala
                130                 135                 140
agt wag atc aag gag aca tgg aag aaa gac aga ngg ctg gaa aak tat     583
Ser Xaa Ile Lys Glu Thr Trp Lys Lys Asp Arg Xaa Leu Glu Xaa Tyr
            145                 150                 155
ttc agg aag ctc tca aar gga gac tgc gat cac tgg ctc agg gaa ttc     631
Phe Arg Lys Leu Ser Lys Gly Asp Cys Asp His Trp Leu Arg Glu Phe
        160                 165                 170
tta ggg cac tgg gaa gca atg cca raa ccg ama gtg tcm cca rta aat     679
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```
Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val Ser Pro Xaa Asn
    175                 180                 185
gct tca raw atc cac tgg tct tct tct art cta cca raw ara tgg atc      727
Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro Xaa Xaa Trp Ile
190                 195                 200                 205
atc ctg ggg gca ttc atc ctg tta vtt tta atg gga att gtt ctc atc      775
Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly Ile Val Leu Ile
                210                 215                 220
tgt gtc tgg tgg caa aat ggc ara ara tcc acc tad arg tgataccacg       824
Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa Xaa
            225                 230
gcggcgcaaa attgttcacc tgtggtcctc gatcgctgac agccttggct cccactgctg    884
tgtgttccct gagtcaagtg gaggcggagc ctgcaatgag cggaratcgc gcctctgcat    944
tccagtcttg gcaacagarc aagactccgt ctcaaaaaaa aaaaa                    989
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<210> 321
<211> 1017
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 3..581

<221> sig_peptide
<222> 3..182
<223> Von Heijne matrix
score 6.69999980926514
seq LWPFLTWINPALS/IC

<221> polyA_site
<222> 1006..1016

<400> 321

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ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg        47
   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu
   -60                 -55                 -50
ccc tgc tca gga caa cag cag cct ttc ccg ttt gga gcc tca aac atc       95
Pro Cys Ser Gly Gln Gln Gln Pro Phe Pro Phe Gly Ala Ser Asn Ile
-45                 -40                 -35                 -30
cca cta ctc ctg ggc agg agc aga aag gtg gct cga ggt gca ccg gtc      143
Pro Leu Leu Leu Gly Arg Ser Arg Lys Val Ala Arg Gly Ala Pro Val
                -25                 -20                 -15
ctg tgg cca ttt ctc act tgg ata aac cct gca ctg tcc atc tgt gac      191
Leu Trp Pro Phe Leu Thr Trp Ile Asn Pro Ala Leu Ser Ile Cys Asp
            -10                 -5                  1
ccc tta gga tcc tgc gga tgg cyw tgc cac acg gcc car gtc cct gcg      239
Pro Leu Gly Ser Cys Gly Trp Xaa Cys His Thr Ala Gln Val Pro Ala
    5                   10                  15
ccc ctg car ttg cct act gcc tgt cct ccc ctc cca cat ggc acc cgg      287
Pro Leu Gln Leu Pro Thr Ala Cys Pro Pro Leu Pro His Gly Thr Arg
20                  25                  30                  35
gct gta ggc ccc acg cca ggc ctc ctc cct gag gct gca gcc cca sgc      335
Ala Val Gly Pro Thr Pro Gly Leu Leu Pro Glu Ala Ala Ala Pro Xaa
                40                  45                  50
acg tgk ggg gca ctg tcc tca cgc agc agg cac tgg tca tgt tcc att      383
Thr Xaa Gly Ala Leu Ser Ser Arg Ser Arg His Trp Ser Cys Ser Ile
            55                  60                  65
gtc arc tgc ctc cac ctg cac ara ctc ctg tct gtg gag acc aga arc      431
Val Xaa Cys Leu His Leu His Xaa Leu Leu Ser Val Glu Thr Arg Xaa
```

```
          70                  75                  80
ttc cas aaa cat ctg ttg gtg ctg ctg gtg gct gtg gcc cat agt gtt      479
Phe Xaa Lys His Leu Leu Val Leu Leu Val Ala Val Ala His Ser Val
    85                  90                  95
ctg gaa cca cct gcc ctg gtc cca aat gtg cag tgt gag atg tgc aca      527
Leu Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr
100                 105                 110                 115
cac tca ggg ccc cgt gac ctg gaa gcc gca gtc gtg tcc cca gca cct      575
His Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro
                120                 125                 130
tgg gaa tgagcctgtc ctctgtgtga aggaggggt ggttctcaaa ccactgactc        631
Trp Glu
ttggtgctca ggaggggcct gctgctgtcc tgggcatggg gtggtcattg ttcaagactg    691
aggcagactc agtctttgaa agggtgcaga ggccaggcgc ggtggctcac gcctgtaatt    751
ccagcacttt gggaggccaa ggtggacaga tcatgaggtc aggagttcga gaccagcctg    811
gccaatacgg tgaaaccgca tctctactaa rraatawcaw aaattagtcg ggcatgggtg    871
atgtgtgctt gtagtcccag ctactcatga ggyctgaggc agaagaatca cctgaatctg    931
ggaggcagag gttgcagtga accaagatcg cacgactgta caccagcctg ggcgacagag    991
tgagactccg tctcaaaaaa aaaaam                                        1017
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<210> 322
<211> 529
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 107..427

<221> sig_peptide
<222> 107..190
<223> Von Heijne matrix
score 3.79999995231628
seq RFLSLSAADGSDG/SH

<221> polyA_signal
<222> 499..504

<221> polyA_site
<222> 516..529

<400> 322

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gaggcgggag gccgmsggmg gagctcttcc tgcaggcgtg garacc atg gtg ctc      115
                                                   Met Val Leu
acg ctc gga gaa agt tgg ccg gta ttg gtg ggg agg agg ttt ctc agt      163
Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg Phe Leu Ser
-25                 -20                 -15                 -10
ctg tcc gca gcc gac ggc agc gat ggc agc cac gac agc tgg gac gtg      211
Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser Trp Asp Val
                -5                  1               5
gag cgc gtc gcc gag tgg ccc tgg ctc tcc ggg acc att cga gct gtt      259
Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile Arg Ala Val
        10                  15                  20
tcc cac acc gac gtt acc aag aag gat ctg aag gtg tgt gtg gaa ttt      307
Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys Val Glu Phe
    25                  30                  35
gak ggg gaa tct tgg agg aaa aga aga tgg ata gaa gtc tac agc ctt      355
Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val Tyr Ser Leu
40                  45                  50                  55
```

```
cta agg aaa gca ttt tta gta aaa cat aat ttg gtt tta gct gaa cga      403
Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu Ala Glu Arg
            60                  65                  70
aag tca cct gaa att tct tgg ggt taaccatctt tagttaaatg gaattttaat     457
Lys Ser Pro Glu Ile Ser Trp Gly
        75
ttaaatgacg ctttgctaat tttaagtgtt aagcattttg cattaaaata ttcatataat   517
aaaaaaaaaa aa                                                        529
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<210> 323
<211> 1046
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 45..407

<221> sig_peptide
<222> 45..83
<223> Von Heijne matrix
score 5.69999980926514
seq MLVLRSALTRALA/SR

<221> polyA_signal
<222> 1008..1013

<221> polyA_site
<222> 1032..1042

<400> 323

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aaaaggacac ggctggctgc ttttctcagc gccgaagccg cgcc atg ctc gtc ctc      56
                                                  Met Leu Val Leu
                                                              -10
aga agc gcc ctg act cgg gcg ctg gcc tca cgg acg ctg gcg cct cag     104
Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr Leu Ala Pro Gln
                -5                  1               5
atg tgc tca tct ttt gct acg gga ccc aga caa tac gat gga ata ttc     152
Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr Asp Gly Ile Phe
        10                  15                  20
tat gaa ttt cgt tct tat tac ctt aag ccc tca aag atg aat gag ttc     200
Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys Met Asn Glu Phe
    25                  30                  35
ctg gaa aat ttt gag aaa aac gct caa ctt cgg aca gct cac tct gaa     248
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu
40                  45                  50                  55
ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg     296
Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val
                60                  65                  70
ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag     344
Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln
            75                  80                  85
aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca     392
Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln Phe Leu Ile Pro
        90                  95                  100
aat ttg gct ctc aat tgataaacaa gatagtgaga ttacttatct ggtaccatgg     447
Asn Leu Ala Leu Asn
    105
tgcaaattag aaaaacctcc aaaagaagga gtctatgaac tggccacttt tcagatgaaa   507
cctggtgggc cagctctgtg ggtgatgca tttaaaaggg cagttcatgc tcatgtcaat    567
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ctaggctaca caaaactagt tggagtgttc cacacagagt acggagcact caacagagtt     627
catgttcttt ggtggaatga gagtgcagat agtcgtgcag ctgggagaca taagtcccat     687
gaggatccca gagttgtggc agctgttcgg gaaagtgtca actacctagt atctcagcag     747
aatatgcttc tgattcctac atcgttttca ccactgaaat agttttctac tgaaatacaa     807
aacatttcat taactgctat aggatctgtc tgctaatggt gcttaaattc tcccaagagg     867
ttctcacttt tatttgaagg aggtggtaag ttaatttgct atgtttcttg cattatgaag     927
gctacatctg tgctttgtaa gtaccacttc aaaaaatakt tctgtttact ttctgcatgg     987
tatttcagtg tctgtcatac attaaaaata cttgtcactg tttyaaaaaa aaaaammcc     1046


<210> 324
<211> 880
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 201..332

<221> sig_peptide
<222> 201..251
<223> Von Heijne matrix
      score 7.80000019073486
      seq VLWLISFFTFTDG/HG

<221> polyA_site
<222> 869..880

<400> 324
aattgctgat ggatcagtga gcctgtgttc atgccagtga gctgctgtgg ctcagatact      60
gatactttct ttccaaacag cataagaagt gattgancca caagtatact gaaggmargg     120
yhcccwsvar tyctggwgtg amgagataaa tcaccagtca cagactatgc acccgactgc     180
tgctgttcag tccagggaaa atg aaa gtt gga gtg ctg tgg ctc att tct ttc     233
                      Met Lys Val Gly Val Leu Trp Leu Ile Ser Phe
                                  -15                 -10
ttc acc ttc act gac ggc cac ggt ggc ttc ctg ggg gtg agt tgg tgc       281
Phe Thr Phe Thr Asp Gly His Gly Gly Phe Leu Gly Val Ser Trp Cys
    -5                  1               5                   10
tat gtc tca tat ctc ttc tca act aac tct cct ctc tcg ttc cgg cgc       329
Tyr Val Ser Tyr Leu Phe Ser Thr Asn Ser Pro Leu Ser Phe Arg Arg
                15                  20                  25
att tagaacccct cactctctag gggactgcaa ctgcataatt taatgtactt            382
Ile
gagatcagaa gtcctgagtt ctcgtttcaa cattaccaac attcactgtg tggccttgga     442
taagtragtc atttcatctc ttcggagctt agatgatcma actgcaarag gaggatcttt     502
gattamacta tcttagagat cttttccagt tcaacacatg ctgtactatg gcttctcgga     562
tgcagaaaaa tcacatggat ggacattagc aatccttara cactgtcttt cctgtctaca     622
ctcgcttgag tgatgckttc atctaggatc atggttttaa tattctctac atgctgatga     682
ctcccagctg tatagctcca tctcagaacc tctcccctgt ccacactcac atatccatta     742
cctacgtgtt atttccagct gggaaatcca gcggaacctc ggnaacttca tttgnttcaa     802
aatcgnaacc caatccttct tgcctatctc agcaagtggt atcactatct ttccagctac     862
ttaggcaaaa aaaaaaa                                                    880


<210> 325
<211> 1217
<212> DNA
<213> Homo sapiens

<220>
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<221> CDS
<222> 217..543

<221> sig_peptide
<222> 217..255
<223> Von Heijne matrix
      score 6.40000009536743
      seq MCLLTALVTQVIS/LR

<221> polyA_site
<222> 1206..1217

<400> 325
aatgccagtg tcagcttctc tccgaaaact gggtaatacg aaatggtctt tattggttgt      60
gaacactcga gctgagaaac attttaggat ctttgtgtct tttgtgatga ttttgtttct     120
graagrwgga aasctgtcta aaaatattca agtgtgcaac caaggattta gatgaagcca     180
gcaaacaaag gaatcatgta atcaggacct gagcga atg tgc tta ctc acg gcg       234
                                        Met Cys Leu Leu Thr Ala
                                                        -10
tta gtt aca cag gtg att tcc tta aga aaa aat gca gag aga act tgt       282
Leu Val Thr Gln Val Ile Ser Leu Arg Lys Asn Ala Glu Arg Thr Cys
        -5                  1               5
tta tgc aag agg aga tgg ccc tgg ngc ccc tcg ccc cgg atc tac tgc       330
Leu Cys Lys Arg Arg Trp Pro Trp Xaa Pro Ser Pro Arg Ile Tyr Cys
10                  15                  20                  25
tca tcc acc cca tgc gat tcc aaa ttc ccc acc gtc tac tcc agt gcc       378
Ser Ser Thr Pro Cys Asp Ser Lys Phe Pro Thr Val Tyr Ser Ser Ala
                30                  35                  40
cca ttc cat gcc ccc ctc ccc gtc cag aat tcc tta tgg ggg cac ccg       426
Pro Phe His Ala Pro Leu Pro Val Gln Asn Ser Leu Trp Gly His Pro
            45                  50                  55
ctc cat ggt tgt tcc tgg caa tgc cac cat ccc cag gga car aat ctc       474
Leu His Gly Cys Ser Trp Gln Cys His His Pro Gln Gly Gln Asn Leu
        60                  65                  70
cag cct gcc agt ctc cad acc cat ctc tcc aag ccc aag cgc cat ttt       522
Gln Pro Ala Ser Leu Xaa Thr His Leu Ser Lys Pro Lys Arg His Phe
    75                  80                  85
ara aar aar rra tgt caa gcc tgatgaarac atgagtggca aaaacattgc          573
Xaa Lys Lys Xaa Cys Gln Ala
90                  95
aatgtacara aatgagggtt tctatgctga tccttacctt tatcacgagg gacggatgag     633
catascctca tcccatggtg gacacccact ggatgtcccc gaccacatca ttgcatatca     693
ccgcaccgcc atccggtcag cgagtgctta ttgtaacccc tcaatgcaag cggaaatgca     753
tatggaacaa tcactgtaca gacagaaatc aaggaaatat ccggatagcc atttgcctac     813
actgggctcc aaaacacccc ctgcctctcc tcacagaktc agtgacctga ggatgataga     873
catgcacgct cactataatg cccacggccc ccctcacacc atgcagccag accgggcctc     933
tccgagccgc caggccttta aaaggagcc aggcaccttg gtgtatatag aaaagccacg      993
gagcgctgca ggattatcca gccttgtaga cctcggccct cctctaatgg agaagcaagt    1053
ttttgcctac agcacggcga caatacccaa agacagagag accagagaga ggatgcaagc    1113
catggagaaa cagattgcca gtttaactgg ccttgttcag tctgcgcttt ttaaagggcc    1173
cattacaagt tatagcaaar atgcgtctag ctaaaaaaaa aaaa                     1217


<210> 326
<211> 959
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 18..446
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<221> sig_peptide
<222> 18..140
<223> Von Heijne matrix
score 4.09999990463257
seq GILILWIIRLLFS/KT

<221> polyA_signal
<222> 930..935

<221> polyA_site
<222> 948..959

<400> 326
aaaggaagcg gctaact atg gcg acc gcc acg gag cag tgg gtt ctg gtg 50
Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val
-40 -35
gag atg gta cag gcg ctt tac gag gct cct gct tac cat ctt att ttg 98
Glu Met Val Gln Ala Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu
-30 -25 -20 -15
gaa ggg att ctg atc ctc tgg ata atc aga ctt ctt ttc tct aag act 146
Glu Gly Ile Leu Ile Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr
-10 -5 1
tac aaa tta caa gaa cga tct gat ctt aca gtc aag gaa aaa gaa gaa 194
Tyr Lys Leu Gln Glu Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu
5 10 15
ctg att gaa gag tgg caa cca gaa cct ctt gtt cct cct gtc cca aaa 242
Leu Ile Glu Glu Trp Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys
20 25 30
gac cat cct gct ctc aac tac aac atc gtt tca ggc cct cca agc cac 290
Asp His Pro Ala Leu Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His
35 40 45 50
aaa act gtg gtg aat gga aaa gaa tgt ata aac ttc gcc tca ttt aat 338
Lys Thr Val Val Asn Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn
55 60 65
ttt ctt gga ttg ttg gat aac cct agg gtt aag gca gca gct tta gca 386
Phe Leu Gly Leu Leu Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala
70 75 80
tct cta aag aag tat ggc gtg ggg act tgt gga ccc tgt gga ttt tat 434
Ser Leu Lys Lys Tyr Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr
85 90 95
ggc aca ttt gaa tgaaratgaa ggatcattga tttccttgtg tatggataat 486
Gly Thr Phe Glu
100
ccgggaacag gccaactaaa tatttgatga atgtatgatt tcaaatacag tgaattccct 546
gggagtcatc aaaraagacg gcattttatg gttgttttta ttaagtgtat attctttgct 606
cctgaaaatg ttattaaata attgtttagg ccgggcatgg tggctcatgc ctgtaatccc 666
agcactttca aaggctgagg caggcagatc acctgaggtc aggagttcaa aaccagcctg 726
gccaacatgc tgaaacctcg tctctactaa aaatacaaaa attagctggg cgtggtggtg 786
grtgcctgtg gtcccagctr cgtgggaggc tgaggtggga gaattgcttc aacctgggag 846
gcggaggttg cagtgagccg agatcatgcc actgcactcc agcctgggca acagagcaag 906
actgtctcaa aaataaataa ataaataaaa ttgtttaaat gaaaaaaaaa aaa 959

<210> 327
<211> 921
<212> DNA
<213> Homo sapiens

<220>
<221> CDS

<222> 29..724

<221> sig_peptide
<222> 29..118
<223> Von Heijne matrix
score 3.90000009536743
seq VAHALSLPAESYG/NX

<221> polyA_signal
<222> 886..891

<221> polyA_site
<222> 910..920

<400> 327
aaggagccac gctttcgggg gttgcaag atg gcg gcc acc agt gga act gat 52
Met Ala Ala Thr Ser Gly Thr Asp
-30 -25

gag ccg gtt tcc ggg gag ttg gtg tct gtg gca cat gcg ctt tct ctc 100
Glu Pro Val Ser Gly Glu Leu Val Ser Val Ala His Ala Leu Ser Leu
-20 -15 -10

cca gca gag tcg tat ggy aac grt yct gac att gag atg gct tgg gcc 148
Pro Ala Glu Ser Tyr Gly Asn Xaa Xaa Asp Ile Glu Met Ala Trp Ala
-5 1 5 10

atg aga gca atg cag cat gct gaa gtc tat tac aag ctg att tca tca 196
Met Arg Ala Met Gln His Ala Glu Val Tyr Tyr Lys Leu Ile Ser Ser
15 20 25

gtt gac cca cag ttc ctg aaa ctc acc aaa gta gat gac caa att tac 244
Val Asp Pro Gln Phe Leu Lys Leu Thr Lys Val Asp Asp Gln Ile Tyr
30 35 40

tct gag ttc cgg aaa aat ttt gag acc ctt agg ata gat gtg ttg grc 292
Ser Glu Phe Arg Lys Asn Phe Glu Thr Leu Arg Ile Asp Val Leu Xaa
45 50 55

cca gaa gan ctc aag tca gaa tca gcn aaa gag ccc cca gga tac aat 340
Pro Glu Xaa Leu Lys Ser Glu Ser Ala Lys Glu Pro Pro Gly Tyr Asn
60 65 70

tct ttg cca ttg aaa ttg ctc gga acc ggg aag gct ata aca aag ctg 388
Ser Leu Pro Leu Lys Leu Leu Gly Thr Gly Lys Ala Ile Thr Lys Leu
75 80 85 90

ttt ata tca gtg ttc agg aca aag aag gag aga aag gag tca aca atg 436
Phe Ile Ser Val Phe Arg Thr Lys Lys Glu Arg Lys Glu Ser Thr Met
95 100 105

gag gag aaa aaa gag ctg aca gtg gag aag aag aga aca cca aga atg 484
Glu Glu Lys Lys Glu Leu Thr Val Glu Lys Lys Arg Thr Pro Arg Met
110 115 120

gag gag aga aag gag ctg ata gtg gag aag aaa aag agg aag gaa tca 532
Glu Glu Arg Lys Glu Leu Ile Val Glu Lys Lys Lys Arg Lys Glu Ser
125 130 135

aca gag aag aca aaa ctg aca aag gag gag aaa aag gga aag aag ctg 580
Thr Glu Lys Thr Lys Leu Thr Lys Glu Glu Lys Lys Gly Lys Lys Leu
140 145 150

aca aag aaa tca aca aaa gtg gtg aaa aag cta tgt aag gta tac agg 628
Thr Lys Lys Ser Thr Lys Val Val Lys Lys Leu Cys Lys Val Tyr Arg
155 160 165 170

gaa cag cac tct aga agc tat gac tca att gag act aca agt acc acg 676
Glu Gln His Ser Arg Ser Tyr Asp Ser Ile Glu Thr Thr Ser Thr Thr
175 180 185

gtg cta ctt gca cag acc cct ttg gtt aaa tgt aaa ttc ttg tac aat 724
Val Leu Leu Ala Gln Thr Pro Leu Val Lys Cys Lys Phe Leu Tyr Asn
190 195 200

tgaaggatac gcagaaggac atctttctag tctaacagtc aggagctgct ctggtcattc 784
ccttgtatga actggtctaa agactgttag tggggtgtta gttgattttt cctggtatac 844

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tgtttcttgg ctgacactac tggtcaagta agaaatttgt aaataaattt cttttggttc     904
ttattaamaa aaaaaas                                                     921


<210> 328
<211> 1344
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 404..586

<221> sig_peptide
<222> 404..466
<223> Von Heijne matrix
      score 4.09999990463257
      seq SLMFFSMMATCTS/NV

<221> polyA_signal
<222> 1304..1309

<221> polyA_site
<222> 1334..1344

<400> 328
ataatttaat gcaaaatatc cttttatgaa tttcatgtta atattgtgaa atattaaaat      60
aattccacaa tagttgagaa aaatgagcat ttttttccat ttttaaaaaa tgcatagaaa     120
agacaatttt aaaatcctgg gamccawatt tatttagaag tagctgttag taaaacatta     180
gaaaaggagt caggccatba ggttatttat nbnaatctct aagcaattag gntgaagtta     240
ttaagtcaag cctagaaaag ctgcctcctt gtaaggcttt catgacaatg tatagtaatc     300
brcagtgtcc aattcttcgc actcctcagg aatatcacta cctcaggtta cggtacacag     360
gctataattg atgatgatgt tcagataact gaagacacaa taa atg aca ttc aga       415
                                                Met Thr Phe Arg
                                                    -20
cat cag gac aat tcc ctc atg ttc ttt tct atg atg gcc acc tgt acc       463
His Gln Asp Asn Ser Leu Met Phe Phe Ser Met Met Ala Thr Cys Thr
        -15                 -10                 -5
agc aac gtg ggt ttc acc cac aca acg atg aac tgt tct ctt act tct       511
Ser Asn Val Gly Phe Thr His Thr Thr Met Asn Cys Ser Leu Thr Ser
  1               5                  10                  15
cca gtt gat ttt aaa gac ttg tta aga gtc tta cta ata aaa ttt ggg       559
Pro Val Asp Phe Lys Asp Leu Leu Arg Val Leu Leu Ile Lys Phe Gly
                20                  25                  30
tat gat aga aaa tcc aca atc aaa tct tgaaccaaat aacatattaa             606
Tyr Asp Arg Lys Ser Thr Ile Lys Ser
            35                  40
attactaata tttaagtgat ggaagacaca caaaaaactt aaaagcacga acaacctaac     666
ttgaaaaara attttaaaat atgattaacc tgaaraaaar araatcctaa ragccaaagc     726
tccttttat ttagcttgga atttcctat tggttcctaa caaactgtcc caatgtcata       786
taaggaaaca tgatctatta cattccttta taacaacgtg gararactat aaacctatgt     846
aagtagtaaa actatatcag adactcagga ractgactww aaggcctgga tctgcagtgt     906
attatctgta taaaaattgg caggggggaag ctaaaaggaa aggagattgg agatctcaat    966
tctatcatgg tgtatttcat acgcaaatca ragcatgcat tgttttttgt ttttggaaar    1026
avaarggaag tgtgttctgc cccatgtttc cttccgtgtt tatagttcaa actctatata    1086
tacttcaggt atttttgtt tagcccttca ttataaatgg gcaggaaatt gtttatcaac     1146
ctagccagtt tattactagt gaccttgact tcagtatctt gagcattctt ttatattttt    1206
ctttattat cctgagtctg taactaaaca attttgtctt caaattttta tccaatatcc     1266
attgcaccac accaaatcaa gcttcttgat tttcaaaaat aaaaaggggg aaatacttac    1326
aacttgtaaa aaaaaaaa                                                  1344
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<210> 329
<211> 585
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 331..432

<221> sig_peptide
<222> 331..387
<223> Von Heijne matrix
score 7
seq AGLSSCLLPLCWL/ER

<221> polyA_signal
<222> 548..553

<221> polyA_site
<222> 573..585

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<400> 329
aagcctaggt gtggcgcccc gaccggactt tcacttctgg ccagcccttt ccccacctgg      60
gcgcgggass ggtgccagtc tttaaacaac ctctcgatgg gtcccacgaa gatgtttcca     120
gacccttgga atgccaagtt caagtttagc tatgtctcgc ggagaggccg gtggaagaag     180
caacgagaat gaagcacccc agttctctgc tgagcacatg ggcatctgca ataaagattt     240
aatttcccag cttctcctga agctcggtat ggccacaaca ctaaattctg cccgaggaga     300
ttgagcaaaa tagtatggga cttccaagaa atg ttt tta aag tca ggg gca ggc      354
                                 Met Phe Leu Lys Ser Gly Ala Gly
                                                     -15
ctt tct tca tgc ctt ctt cct ctt tgc tgg ctg gaa cgc aaa gac cat      402
Leu Ser Ser Cys Leu Leu Pro Leu Cys Trp Leu Glu Arg Lys Asp His
    -10                 -5                  1               5
ggc agg agg cca agc asc cat cct gga agg tgaaagcctc atactaagga        452
Gly Arg Arg Pro Ser Xaa His Pro Gly Arg
                10                  15
cgtcaracag cgaaataara rcctgggtcc ttgaccctgt aaasatctcc ctccccatcc     512
tggtctgtct gccttgactc ctttcatatg aaaaaaataa acttttaact tgcgtwaacc     572
aaaaaaaaaa aaa                                                        585
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<210> 330
<211> 914
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 59..703

<221> sig_peptide
<222> 59..220
<223> Von Heijne matrix
score 5.09999990463257
seq FLLSQMSQHQVHA/VQ

<221> polyA_signal
<222> 886..891

<221> polyA_site
<222> 903..914

<400> 330
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acaaatatca atgatgttta tgaatctagt gtgaaagtkt taatcacatc acaaggct        58
atg aac rra tat gca agt cca ttc aac tgw caa ttg ard tat ttg gak       106
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa
                -50                 -45                 -40
ttg agc agr ttc gag tgt gtr cat aga gat gga aga gta att aca ctg       154
Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val Ile Thr Leu
            -35                 -30                 -25
tct tat cag gag cag gag cta cag gat ttt ctt ctg tct cag atg tca       202
Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln Met Ser
        -20                 -15                 -10
cag cac cag gta cat gca gtt cag caa ctc gcc aag gtt atg ggc tgg       250
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp
    -5                  1               5                   10
caa gta ctg agc ttc agt aat cat gtg gga ctt gga cct ata gag agc       298
Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser
                15                  20                  25
abt ggt aat gca tct gcc atc acg gtg gcc ccc caa gtg gtg act atg       346
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met
            30                  35                  40
cta ttt cag ttc gta atg gac ctg aaa gtg gca gca aga tta tgg ttc       394
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe
        45                  50                  55
agt ttc ctc gta acc aat gta aar acc ttc caa aaa gtg atg ttt tac       442
Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gln Lys Val Met Phe Tyr
    60                  65                  70
aar ata aca aat gga gtc atc ttc gtg ggc cat tca aar aag ttc agt       490
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser
75                  80                  85                  90
gga ata aaa tgg aag gtc kaa att ttg ttt ata aaa tgg arm tgc tta       538
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu
                95                  100                 105
tgt ctg cac tta gcc ctt gtc tac tat gat ttt ttc car atg ttt cct       586
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro
            110                 115                 120
aaa raa gtt tcc ara aac ttt gac ttg aaa tgt ttg car atc aac tat       634
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr
        125                 130                 135
aag cac aaa gaa gar ata act tcc aaa aga gtg ctg ttt tta aaa ata       682
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys Ile
    140                 145                 150
ata att agg aaa tgt ttt att tagcactttc aaactttca ctttataaat          733
Ile Ile Arg Lys Cys Phe Ile
155                 160
gacaagtgct ttgaaatgca gaagtttatg tacagttgta tatacagtat gacaagatgt    793
aaaataatat gtttttcatg cagtttaaaa tattactaac ttaagggttt ctatgtgctt    853
tttaaaatat tccttctttg atgttgacat caaataaagt atgtggttta aaaaaaaaaa    913
a                                                                    914
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<210> 331
<211> 1161
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 672..752

<221> sig_peptide
<222> 672..722
<223> Von Heijne matrix
score 4.30000019073486
seq LLYAHLSFTSKRA/VV

<221> polyA_site
<222> 1150..1161

<400> 331
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aagatatcac tgtcttgttt tcacttagat cctacttaca aagtgagggt tattaacaga      60
ataaagcctt cctttaaagc tttataataa tcatatttat taataatgct gttgtgcata     120
cttatagtat gcatatattc agcatatgtt gcatgtsttc agaattacat aagatgaaat     180
ccctttcatt gcaacttgca agtgagaaaa gatccttagt ggctctggtg gaagaaatag     240
tatttcttct tctcagggtg tctccctgcc ttggcccctc ccagaagccc cggctttaaa     300
agtgaaaatg tttgaaacat gaaacatgtc tgtaggaagc atcagcatgg ccataagtgc     360
artgattttc atatatgcct ctgcccattt caaatatatt tttgacatga ataaatctaa     420
cagtatacar aataattcat gtaaraccct aacgtgtaca tgtgaaaaag catttctata     480
taatgtgagg agcactggcc atcaattagg gaaataaagg tcatgtaata ttgcaaattt     540
tcaaaataga gcsstgcaag ataactgcaa tcataccaaa aactatttga gtaaatggat     600
ttttaaagta atttttgttt aaaaaaattt atatttcaga agsagaaaat gtcaaatgat     660
agtctttgta a atg gtg gtg cac ctt ctc tat gca cat ctg tct ttt aca      710
             Met Val Val His Leu Leu Tyr Ala His Leu Ser Phe Thr
                     -15                 -10                 -5
tca aaa aga gct gtg gtc atg cta aaa tta gag ata act ttt               752
Ser Lys Arg Ala Val Val Met Leu Lys Leu Glu Ile Thr Phe
                1               5                  10
tgaatgactt ggtcaagctg tgtgtaaaat atttaaccat aagtcaagta cagtgtacta     812
tgtttaataa agttacattt aatgcattta ttgcatatat gaatatatac atgaagaggc     872
tttatgtctt ctggtatttg attttgaatg ttttttaagt cagtggtgcc tttaggcaag     932
aactttcgaa attaatcatt ctttgtgttt tctgattttt caggtaacat gtacactatt     992
tagaaaccat catagtttat tcaccttaaa aaattgattg tattatttaa atatatcact    1052
tagatgggca tttcctataa ttaggatatt ccaaatagtt gctgaaatca attgtgccat    1112
tgaccaatgg atgcacttgg ttagccttaa ttttttyaaa aaaaaaaaa                1161
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<210> 332
<211> 363
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 57..311

<221> sig_peptide
<222> 57..128
<223> Von Heijne matrix
score 5.30000019073486
seq LFHLLFLPHYIET/FK

<221> polyA_signal
<222> 332..337

<221> polyA_site
<222> 351..363

<400> 332
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acatttctta ctgccttacg ctcatcctga ggtccacctt ggtctctaaa aacacc atg      59
                                                              Met
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tgt tct cat gcc tcc atg tct ttt cac aca ctg ttc cat ttg ctc ttc 107
Cys Ser His Ala Ser Met Ser Phe His Thr Leu Phe His Leu Leu Phe
-20 -15 -10
ctc cca cat tac att gaa act ttc aag cct cag tcg aaa cat tgc ttc 155
Leu Pro His Tyr Ile Glu Thr Phe Lys Pro Gln Ser Lys His Cys Phe
-5 1 5
ttc tgg ata gca gcc ttc ttg aca tcc ctc ctc act ccc cag tcc cta 203
Phe Trp Ile Ala Ala Phe Leu Thr Ser Leu Leu Thr Pro Gln Ser Leu
10 15 20 25
cag ggc ttc cat agc tct tta tgt gca ctt cga tcc cag cat ttt cca 251
Gln Gly Phe His Ser Ser Leu Cys Ala Leu Arg Ser Gln His Phe Pro
30 35 40
tcg act tgt aat tgt ttc tgc tac ctg aca atc atc gcc ttg drd tac 299
Ser Thr Cys Asn Cys Phe Cys Tyr Leu Thr Ile Ile Ala Leu Xaa Tyr
45 50 55
tgg gac aac ctt tgattactca ttatatcctc aataaatatt tgttgaacca 351
Trp Asp Asn Leu
60
aaaaaaaaaa aa 363

<210> 333
<211> 645
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 80..232

<221> sig_peptide
<222> 80..127
<223> Von Heijne matrix
score 3.70000004768372
seq IALTLIPSMLSRA/AG

<221> polyA_signal
<222> 617..622

<221> polyA_site
<222> 634..645

<400> 333
acttcttgt tatttatgct attctctttg tggctccatt cttctttcaa tcttctcagc 60
ttataaccgt ctttcccctt atg cta agg ata gcc ctt aca ctc atc cca tct 112
Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser
-15 -10
atg ctg tca agg gct gct ggt tgg tgc tgg tac aag gag ccc act cag 160
Met Leu Ser Arg Ala Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln
-5 1 5 10
cag ttt tct tac ctt tgc ctg ccc tgc ctt tca tgg aat aar aaa ggc 208
Gln Phe Ser Tyr Leu Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly
15 20 25
aac gtt ttg cag ctt cca aat ttc tgaaraaact aatctcarat tggcagttaa 262
Asn Val Leu Gln Leu Pro Asn Phe
30 35
agtcaaaatg ttgccaaata tttattcctt ttgcctaakt ttggctaccc ggttcaattg 322
ctttttattt ttaatgtctt gactcttcar agttcgtacc tcaaaaraac aatgaraaca 382
tttgctttgc tttctgctga atccctaatc tcaacaatct atacctggac tgtccagttc 442
tcctcctgtg ctatcttctc ttctatccaa gtaraatgta ygccaggarc tccttccctc 502
tarcaatttc tactaaaatg tccaagtara atgtttcctt ttacaatcaa attactgtat 562

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ttattaattt gctaraatcc aktaaatcat tttggtagct ctggctgtgc tatcaataaa     622
aagatgaaag caaaaaaaaa aaa                                             645


<210> 334
<211> 400
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 91..291

<221> sig_peptide
<222> 91..219
<223> Von Heijne matrix
      score 3.79999995231628
      seq LISVLYLIPKTLT/TN

<221> polyA_signal
<222> 367..372

<221> polyA_site
<222> 389..400

<400> 334
aacaaaagga gagttttata attcacttta aaaggagatt tgatggtaaa gtttaaagat      60
taaaatattt tgttcttcaa ttacagagcg atg acc cca cag tat ctg cct cac     114
                                 Met Thr Pro Gln Tyr Leu Pro His
                                                 -40
ggt gga aaa tac caa gtt ctt gga gat tac tct ttg gca gtg gtc ttc      162
Gly Gly Lys Tyr Gln Val Leu Gly Asp Tyr Ser Leu Ala Val Val Phe
-35                 -30                 -25                 -20
ccc ctg cac ttt tct gat cta att tct gtt tta tac ctt ata ccc aaa      210
Pro Leu His Phe Ser Asp Leu Ile Ser Val Leu Tyr Leu Ile Pro Lys
                -15                 -10                 -5
aca ctt act acc aac aca gct gtt aaa cat tct ata caa aaa aat tgt      258
Thr Leu Thr Thr Asn Thr Ala Val Lys His Ser Ile Gln Lys Asn Cys
            1               5                   10
atg mat ctg gta tta gga aaa tta ctt tca cag taaatatcaa agaaaaaaga    311
Met Xaa Leu Val Leu Gly Lys Leu Leu Ser Gln
    15                  20
ttaagggtct ctttgccatg cttttcatca tatgcaccaa atgtaaattt tgtacaataa    371
aatttatatt cctaagyaaa aaaaaaaaa                                      400


<210> 335
<211> 496
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 196..384

<221> sig_peptide
<222> 196..240
<223> Von Heijne matrix
      score 6.69999980926514
      seq ILSTVTALTFARA/LD
```

<221> polyA_signal
<222> 461..466

<221> polyA_site
<222> 485..496

<400> 335
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aaaaaattgg tcccagtttt caccctgccg cagggctggc tggggagggc agcggtttag      60
attagccgtg gcctaggccg tttaacgggg tgacacgagc htgcagggcc gagtccaagg     120
cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag     180
gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt      231
                 Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe
                 -15                 -10                 -5
gcc aga gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt       279
Ala Arg Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser
            1               5                   10
gag aag cac aga ctc gag aaa tgt agg gaa ctc gag agc agc cac tcg       327
Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser
    15                  20                  25
gcc cca gga tca acc cag cac cga aga aaa aca acc aga aga aat tat       375
Ala Pro Gly Ser Thr Gln His Arg Arg Lys Thr Thr Arg Arg Asn Tyr
30                  35                  40                  45
tct tca gcc tgaaatgaak ccgggatcaa atggttgctg atcaragccc               424
Ser Ser Ala
atatttaaat tggaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc     484
aaacaaaaaa aa                                                         496
```

<210> 336
<211> 968
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 54..590

<221> sig_peptide
<222> 54..227
<223> Von Heijne matrix
score 3.5
seq GGILMGSFQGTIA/GQ

<221> polyA_site
<222> 955..965

<400> 336
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atatttgccc cttactttat cttgtgcctt gagaaattgc tggggagaga ggt atg         56
                                                           Met
tcc act ggg cag ctg tac agg atg gag gat ata ggg cgt ttc cac tcc       104
Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His Ser
        -55                 -50                 -45
cag cag cca ggt tcc ctc acc cca agc tca ccc act gtt ggg gag att       152
Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu Ile
    -40                 -35                 -30
atc tac aat aac acc aga aac aca ttg ggg tgg att ggg ggt atc ctt       200
Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile Leu
-25                 -20                 -15                 -10
atg ggt tct ttt cag gga acc att gct gga caa ggc aca gga gcc acc       248
Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala Thr
```

-5 1 5
tcc att tct gag ctc tgc aag gga caa gaa cta gag cca tca ggg gct 296
Ser Ile Ser Glu Leu Cys Lys Gly Gln Glu Leu Glu Pro Ser Gly Ala
10 15 20
ggg ctc act gtg gcc cca ccc caa gcc gtc agc ctc cag ggw atc tac 344
Gly Leu Thr Val Ala Pro Pro Gln Ala Val Ser Leu Gln Gly Ile Tyr
25 30 35
acc ctg cct tgg ctg cta cag ctt ttt cac tcc act gcc cta rgg gna 392
Thr Leu Pro Trp Leu Leu Gln Leu Phe His Ser Thr Ala Leu Xaa Xaa
40 45 50 55
dtt cag caa cct aat gga tct cta tct ctg aac atc tct tca tcc cat 440
Xaa Gln Gln Pro Asn Gly Ser Leu Ser Leu Asn Ile Ser Ser Ser His
60 65 70
gct ccr rgt cca rca acc tgc acc ctg gaa cca gga gtg gac cct acc 488
Ala Pro Xaa Pro Xaa Thr Cys Thr Leu Glu Pro Gly Val Asp Pro Thr
75 80 85
cga sct gtc tgt att aat ccc cat ccc cca cca cca atc tta aaa abc 536
Arg Xaa Val Cys Ile Asn Pro His Pro Pro Pro Pro Ile Leu Lys Xaa
90 95 100
cct ctg tcc ccc tac cct aaa ccc cag tta ggt acc cat gct ggg caa 584
Pro Leu Ser Pro Tyr Pro Lys Pro Gln Leu Gly Thr His Ala Gly Gln
105 110 115
gtc aat taacaattta tgcacaggta ctagttttat tgtattaccg ttccagggta 640
Val Asn
120
gctttgaaaa aagtatctca aaaaggcaac atgggccgag cgcagtggct cacgcctgta 700
atcccagcac tttgggaggc caaggtgggc agatcgcctg aggtctggag ttcaagacca 760
gcctggccaa cagggtgaaa ccccgtctct acaaaaatar gaaaattrgc caggtgtggt 820
ggcagacgtc tgtrgtccca gctattcagg agactgaggc acgagaattc catgaaccca 880
ggatgcggag gttgcagtga gccgagattg tgccactgcg ctccagcctg ggcgacagag 940
tggtattctg tttcaaaaaa aaaaamcm 968

<210> 337
<211> 901
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 133..846

<221> sig_peptide
<222> 133..345
<223> Von Heijne matrix
score 9.39999961853027
seq VVSFLLLLAGLIA/TY

<221> polyA_site
<222> 890..901

<400> 337
aagcagcttc caggatcctg agatccggag cagccggggt cggagcggct cctcaagagt 60
tactgatcta tnnatggcag agaaaaaaaa attgtgacca gagacgtgta gcaatgaaca 120
aggaacrtca ta atg rwn nnk ttc aca gac ccc tct tca gtg aat gaa aag 171
Met Xaa Xaa Phe Thr Asp Pro Ser Ser Val Asn Glu Lys
-70 -65 -60
aag agg agg gag cgg gaa gaa agg cag aat att gtc ctg tgg aga cag 219
Lys Arg Arg Glu Arg Glu Glu Arg Gln Asn Ile Val Leu Trp Arg Gln
-55 -50 -45
ccg ctc att acc ttg cag tat ttt tct ctg gaa atc ctt gta atc ttg 267

```
Pro Leu Ile Thr Leu Gln Tyr Phe Ser Leu Glu Ile Leu Val Ile Leu
        -40                 -35                 -30
aag gaa tgg acc tca aaa tta tgg cat cgt caa agc att gtg gtg tct      315
Lys Glu Trp Thr Ser Lys Leu Trp His Arg Gln Ser Ile Val Val Ser
    -25                 -20                 -15
ttt tta ctg ctg ctt gct ggg ctt ata gct acg tat tat gtt gaa gga      363
Phe Leu Leu Leu Leu Ala Gly Leu Ile Ala Thr Tyr Tyr Val Glu Gly
-10                 -5                  1               5
gtg cat caa cag tat gtg caa cgt ata gag aaa cag ttt ctt ttg tat      411
Val His Gln Gln Tyr Val Gln Arg Ile Glu Lys Gln Phe Leu Leu Tyr
            10                  15                  20
gcc tac tgg ata ggc tta gga att ttg tct tct gtt ggg ctt gga aca      459
Ala Tyr Trp Ile Gly Leu Gly Ile Leu Ser Ser Val Gly Leu Gly Thr
        25                  30                  35
ggg ctg cac acc ttt ctg ctt tat ctg ggt cca cat ata gcc tca gtt      507
Gly Leu His Thr Phe Leu Leu Tyr Leu Gly Pro His Ile Ala Ser Val
    40                  45                  50
aca tta gct gct tat gaa tgc aat tca gtt aat ttt ccc gaa cca ccc      555
Thr Leu Ala Ala Tyr Glu Cys Asn Ser Val Asn Phe Pro Glu Pro Pro
55                  60                  65                  70
tat cct gat cag att att tgt cca gat gaa gag ggc act gaa gga acc      603
Tyr Pro Asp Gln Ile Ile Cys Pro Asp Glu Glu Gly Thr Glu Gly Thr
                75                  80                  85
att tct ttg tgg agt atc atc tca aaa gtt agg att gaa gcc tgc atg      651
Ile Ser Leu Trp Ser Ile Ile Ser Lys Val Arg Ile Glu Ala Cys Met
            90                  95                  100
tgg ggt atc ggt aca gca atc gga gag ctg cct cca tat ttc atg gcc      699
Trp Gly Ile Gly Thr Ala Ile Gly Glu Leu Pro Pro Tyr Phe Met Ala
        105                 110                 115
aga gca gct cgc ctc tca ggt gct gaa cca gat gat gaa gag tat cag      747
Arg Ala Ala Arg Leu Ser Gly Ala Glu Pro Asp Asp Glu Glu Tyr Gln
    120                 125                 130
gaa ttt gaa gag atg ctg gaa cat gca gag tct gca caa gta aga aca      795
Glu Phe Glu Glu Met Leu Glu His Ala Glu Ser Ala Gln Val Arg Thr
135                 140                 145                 150
gtg ggg ata gaa aat aga aca ctt tac ttc ttc cta aag agg cta tta      843
Val Gly Ile Glu Asn Arg Thr Leu Tyr Phe Phe Leu Lys Arg Leu Leu
                155                 160                 165
agg taaaattgtt agtagttact ctgaagaaga aaactgctaa agtaaaaaaa aaaaa     901
Arg
```

<210> 338
<211> 1347
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 138..671

<221> sig_peptide
<222> 138..248
<223> Von Heijne matrix
score 3.5
seq LVFNFLLILTILT/IW

<221> polyA_signal
<222> 1319..1324

<221> polyA_site

<222> 1338..1347

<400> 338
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aagaatgctt gtgaagtagc aactaaagtg gcagtgtttc ttctgaaatt ctcaggcagt     60
cagactgtct taggcaaatc ttgataaaat agcccttatc caggttttta tctaaggaat    120
cccaagaaga ctgggga atg gag aga cag tca agg gtt atg tca gaa aag      170
                   Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys
                               -35                 -30
gat gag tat cag ttt caa cat cag gga gcg gtg gag ctg ctt gtc ttc      218
Asp Glu Tyr Gln Phe Gln His Gln Gly Ala Val Glu Leu Leu Val Phe
    -25                 -20                 -15
aat ttt ttg ctc atc ctt acc att ttg aca atc tgg tta ttt aaa aat      266
Asn Phe Leu Leu Ile Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn
-10                  -5                   1               5
cat cga ttc cgc ttc ttg cat gaa act gga gga gca atg gtg tat ggc      314
His Arg Phe Arg Phe Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly
             10                  15                  20
ctt aya atg gga cta att tta csa tat gct aca gca cca act gat att      362
Leu Xaa Met Gly Leu Ile Leu Xaa Tyr Ala Thr Ala Pro Thr Asp Ile
        25                  30                  35
gaa agt ggr rct gtc tat gac tgt gta aaa cta act ttc agt cca tca      410
Glu Ser Gly Xaa Val Tyr Asp Cys Val Lys Leu Thr Phe Ser Pro Ser
    40                  45                  50
act ctg ctg gtt aat atc act gac caa gtt tat gar tat aaa tac aar      458
Thr Leu Leu Val Asn Ile Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys
55                  60                  65                  70
aga gaa ata agt cag cac amc atc aat cct cat cam gga aat gct ata      506
Arg Glu Ile Ser Gln His Xaa Ile Asn Pro His Xaa Gly Asn Ala Ile
                75                  80                  85
ctt gaa aag atg aca ttt gat cca raa atc ttc ttc aat gtt tta ctg      554
Leu Glu Lys Met Thr Phe Asp Pro Xaa Ile Phe Phe Asn Val Leu Leu
            90                  95                 100
cca cca att ata ttt cat gca gga tat agt cta aag aag aga cac ttt      602
Pro Pro Ile Ile Phe His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe
        105                 110                 115
ttt caa aac tta gga tct att tta acg tat gcc ttc ttg gga act gcc      650
Phe Gln Asn Leu Gly Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala
    120                 125                 130
atc tcc tgc atc gtc ata ggg taagtgacat tcggagctca agttgcaggt        701
Ile Ser Cys Ile Val Ile Gly
135                 140
ggctgtgggg tcygtgatct gtgtgaggga tctaacactt ccaggattct tgctggckgg    761
gaaaattgtc tttttttar tawatcacaw atttgtatgt tttttcwgac ttaattccac     821
ggcttckgam aaatacaagg cttcaaatca aagcaaacta waggattgct ggactttctc    881
tgtgagttct ggacttctga cttagggaat gtggatcact tgccttgagt tatgtgaagc    941
gcattgcatt cttcttttag tttgagtaat sccgatatgc tcactgcatt ctttttgtc    1001
ttgtattgag agaccttacc tgtatttggc aggagtgcaa aagtaactat atgccaagag   1061
ttttcttct aaaggaaagt ttacaagaca gcagtctgaa acagatatgt ccaaatatca    1121
acagagttgc ttaatacagg gatagctttt cagttaatac cctgtagaat gcagactctt   1181
tttttcattg tattttcttg attatgctac tgagccctaa gtcacacgtt atatactctg   1241
gcttgcagct catcataaag taaaatgtgg taccaaatgg tgaaggcaat ccagcctctg   1301
ataatcccgt ccaatacatt aaagctccac tgcaggaaaa aaaaaa                  1347
```

<210> 339
<211> 987
<212> DNA
<213> Homo sapiens

<220>
<221> CDS

<222> 124..411

<221> sig_peptide
<222> 124..186
<223> Von Heijne matrix
score 6.30000019073486
seq MVALCCCLWKISG/CE

<221> polyA_signal
<222> 948..953

<221> polyA_site
<222> 971..983

<400> 339

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aagacgctgc ctttagggag agataaaaag cataatgaca ttagctagga aagttaattt      60
tcagttctta ctgaagtgct gtatgaaact gaaatttcca aggaactgaa ttttgtgagc     120
caa atg agc atg caa ttc ttg ttt aag atg gtg gcc tta tgc tgt tgt       168
    Met Ser Met Gln Phe Leu Phe Lys Met Val Ala Leu Cys Cys Cys
        -20                 -15                 -10
ctc tgg aag atc tcc ggc tgt gag gaa gtc cct cta act tac aac ctg       216
Leu Trp Lys Ile Ser Gly Cys Glu Glu Val Pro Leu Thr Tyr Asn Leu
    -5                  1               5                   10
ctc aag tgc ctc cta gat aaa gcg cac tgt gta ctc ctg aca cct tgt       264
Leu Lys Cys Leu Leu Asp Lys Ala His Cys Val Leu Leu Thr Pro Cys
                15                  20                  25
ggt tac atc ttt tcc ttg atc agt cca gaa att ctc aaa ctc act tta       312
Gly Tyr Ile Phe Ser Leu Ile Ser Pro Glu Ile Leu Lys Leu Thr Leu
            30                  35                  40
atc act ttg cav atc ctc tta ata ctc aaa aat cta cac tta ctg tgg       360
Ile Thr Leu Xaa Ile Leu Leu Ile Leu Lys Asn Leu His Leu Leu Trp
        45                  50                  55
ctg aca gtt tca agc awa tgt gtt cat cgc agt agt gca aga aaa gaa       408
Leu Thr Val Ser Ser Xaa Cys Val His Arg Ser Ser Ala Arg Lys Glu
    60                  65                  70
aag tagaagaacc ctgcagagat ttgatggaac ccagcttcta ttcattaaaa            461
Lys
75
ccaatggcaa aatataaagc aaataggagg tgacgaaggt tacaaaaata cgtattgttt     521
atgttttccc tggggtgtgc tgattgtcag gcatcagttc cctgtgccat tcattcccca     581
acacagcatg catcagaaat tttatcaata aatgctttct ctctcaatgt tcaacctatg     641
ctgatagacc attaaataca gtttttgggt tcacagcttg tcatcatcat ttgtctatac     701
ctgtggcaaa gaatatctaa taagatactc tcagcatttt gcacacttaa actaagatgc     761
tgaatgctgt attttacgga ataatcagcc acattaaatt tggagactca acaagcatgc     821
tgtgaacatt caacattagg tttaaatttt atttttaaaa gttaataata aaaggatata     881
tgttaagtat tatgaaaccc tgcatatact gtaataaaat ggtggatgtg aatggacaat     941
atatgcaata aaatttataa tttgattcya aaaaaaaaaa aamccv                    987
```

<210> 340
<211> 748
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 372..494

<221> sig_peptide
<222> 372..443
<223> Von Heijne matrix

score 5.30000019073486
seq RILLLHFYCLLRS/SE

<221> polyA_signal
<222> 708..713

<221> polyA_site
<222> 732..745

<400> 340
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acatgaaatg tgcttggtct gtgatctctt ggtcagatat ctgccttcca ggcgatcctt      60
tgaggttgtg taattcagct ggccctggct cctggtccct gttactgagc tgggcagtcg     120
aaccgaaggc agatgagctc aagatcatgc cttgggaagc atggtgctct aggggtgcct     180
ttttattcct ttcattgtat tatagactgt ttccaagttt atggttagaa atggtaaagt     240
gggtctggtg ttttgaggta gaacccagcc tagggcaaga tatgaactgt tcttgaggta     300
gaaatgtcta cagtcagttg tttcatctag cttgcatctt aaaacacaaa cccttcagtt     360
gctttcactt a atg cac aca ttt gcc aat gac aga ggg tta tac agg atc      410
             Met His Thr Phe Ala Asn Asp Arg Gly Leu Tyr Arg Ile
                             -20                 -15
ctt ctt tta cat ttc tat tgt ctg cta cgc tca tca gag tat att ttg       458
Leu Leu Leu His Phe Tyr Cys Leu Leu Arg Ser Ser Glu Tyr Ile Leu
    -10                 -5                  1               5
ggg tac aag gtt ttg ggg gtt ttt tty ccc att ttg taactgcctt            504
Gly Tyr Lys Val Leu Gly Val Phe Phe Pro Ile Leu
                10                  15
attgaaaadt aaktgccctt ccattccagg cctcctcata ttgtacttgt ttcctgccaa     564
atctggggga tcatttgtat tttaactttg taatctatgg ctctgtactg ttgaaagstc     624
tcaattctgt ggggtctcct tagtatgtat gtgacttttc atgttgcaat atcacacgat     684
gggatggccc gacttttgct cttaataaat aatctgaatg agtaagaraa aaaaaaaaaa     744
accc                                                                  748
```

<210> 341
<211> 1106
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 112..450

<221> sig_peptide
<222> 112..192
<223> Von Heijne matrix
score 7.19999980926514
seq SLLFFLLLEGGXT/EQ

<221> polyA_signal
<222> 1053..1058

<221> polyA_site
<222> 1095..1106

<400> 341
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aagacctcgg aacgagagcg ccccggggag ctcggagcgc gtgcacgcgt ggcavacgga      60
gaaggcvakk rcnnnnrctt gaaggttctg tcaccttttg cagtggtcca a atg aga     117
                                                         Met Arg
raa aag tgg aaa atg gga ggc atg aaa tac atc ttt tcg ttg ttg ttc       165
Xaa Lys Trp Lys Met Gly Gly Met Lys Tyr Ile Phe Ser Leu Leu Phe
-25                 -20                 -15                 -10
ttt ctt ttg cta gaa gga ggc kaa aca gag caa gtr amn cat tca gag       213
```

```
Phe Leu Leu Leu Glu Gly Gly Xaa Thr Glu Gln Val Xaa His Ser Glu
                -5                  1                   5
aca tat tgc atg ttt caa gac aag aag tac aga gtg ggt gag aga tgg      261
Thr Tyr Cys Met Phe Gln Asp Lys Lys Tyr Arg Val Gly Glu Arg Trp
        10                  15                  20
cat cct tac ctg gaa cct tat ggg ttg gtt tac tgc gtg aac tgc atc      309
His Pro Tyr Leu Glu Pro Tyr Gly Leu Val Tyr Cys Val Asn Cys Ile
    25                  30                  35
tgc tca gag aat ggg aat gtg ctt tgc agc cga gtc aga tgt cca aat      357
Cys Ser Glu Asn Gly Asn Val Leu Cys Ser Arg Val Arg Cys Pro Asn
40                  45                  50                  55
gtt cat tgc ctt tct cct gtg cat att cct cat ctg tgc tgc cct cgc      405
Val His Cys Leu Ser Pro Val His Ile Pro His Leu Cys Cys Pro Arg
                60                  65                  70
tgc cca gaa gac tcc tta ccc cca gtg aac aat rwg gtg acc agc          450
Cys Pro Glu Asp Ser Leu Pro Pro Val Asn Asn Xaa Val Thr Ser
            75                  80                  85
tagtcttgck agtacaatgg gacaacttac caacatggas agctgttcgt agctgrrggg    510
ctctttcaga atcggcaacc cmatcaatgc acccagtgca gctgttcgga rggaaacktg    570
tattgtggtc tcaagacttg ccccaaatta acctgtgcct tcccagtctc tgttccarat    630
tcctgctgcc gggtwtgcag argagatgga caactgtcat gggaacmttc tgatggtgat    690
atcttccggc aacctgccaa cagagaagca agacattctt accaccgctc tcactatgat    750
cctccaccaa gccgacaggc tggaggtctg tcccgctttc ctggggccag aagtcaccgg    810
ggagctctta tggattccca gcaagcatca ggaaccattg tgcaaattgt catcaataac    870
aaacacaagc atggacaagt gtgtgtttcc aatggaaaga cctattctca tggcgagtcc    930
tggcacccaa acctccgggc atttggcatt gtggagtgtg tgctatgtac ttgtaatgtc    990
accaagcaag agtgtaagaa aatccactgc cccaatcgat accсctgcaa gtatcctcaa   1050
aaaatagacg gaaaatgctg caaggtgtgt ccaggtaaaa aagcaaaaaa aaaaaa       1106
```

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<210> 342
<211> 1191
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 117..866

<221> sig_peptide
<222> 117..170
<223> Von Heijne matrix
      score 10.6999998092651
      seq LILLALATGLVGG/ET

<221> polyA_signal
<222> 1159..1164

<221> polyA_site
<222> 1178..1190

<400> 342
aaaacccagc ctacctgctg tagctgccgc cactgccgtc tccgccgcca ctggwccccc     60
agagcbnmag ccccagagcc taggaacctg gggcccgctc ctccccсctc caggcc atg    119
                                                              Met
agg att ctg cag tta atc ctg ctt gct ctg gca aca ggg ctt gta ggg      167
Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val Gly
    -15                 -10                 -5
gga gag acc agg atc atc aag ggg ttc gag tgc aag cct cac tcc cag      215
Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser Gln
    1               5                   10                  15
```

```
ccc tgg cag gca gcc ctg ttc gag aag acg cgg cta ctc tgt ggg gcg      263
Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly Ala
                20                  25                  30
acg ctc atc gcc ccc aga tgg ctc ctg aca gca gcc cac tgc ctc aag      311
Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu Lys
            35                  40                  45
ccc cgc tac ata ktt cac ctg ggg cag cac aac ctc cag aag gag gag      359
Pro Arg Tyr Ile Xaa His Leu Gly Gln His Asn Leu Gln Lys Glu Glu
        50                  55                  60
ggc tgt gag car acc cgg aca gcc act gag tcc ttc ccc cac ccc ggc      407
Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro Gly
    65                  70                  75
ttc aac aac agc ctc ccc aac aaa gac cam mgc aat gac atc atg ctg      455
Phe Asn Asn Ser Leu Pro Asn Lys Asp Xaa Xaa Asn Asp Ile Met Leu
80                  85                  90                  95
gtg aak atg gma tcg cca gtc tcc atc acc tgg gct gtg cga ccc ctc      503
Val Xaa Met Xaa Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro Leu
                100                 105                 110
acc ctc tcc tca cgc tgt gtc act gct ggc acc agc tgc ctc att tcc      551
Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile Ser
            115                 120                 125
ggc tgg ggc agc acg tcc agc ccc cag tta cgc ctg cct cac acc ttg      599
Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr Leu
        130                 135                 140
cga tgc gcc aac atc acc atc att gag cac cag aag tgt gag aac gcc      647
Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn Ala
    145                 150                 155
tac ccc ggc aac atc aca gac acc atg gtg tgt gcc agc gtg cag gaa      695
Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln Glu
160                 165                 170                 175
ggg ggc aag gac tcc tgc cag ggt gac tcc ggg ggc cct ctg gtc tgt      743
Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
                180                 185                 190
aac cag tct ctt caa ggc att atc tcc tgg ggc cag gat ccg tgt gcg      791
Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys Ala
            195                 200                 205
atc acc cga aag cct ggt gtc tac acg aaa gtc tgc aaa tat gtg gac      839
Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val Asp
        210                 215                 220
tgg atc cag gag acg atg aag aac aat tagactggac ccacccacca            886
Trp Ile Gln Glu Thr Met Lys Asn Asn
    225                 230
cagcccatca ccctccattt ccacttggtg tttggttcct gttcactctg ttaataagaa    946
accctaagcc aagaccctct acgaacattc tttgggcctc ctggactaca ggagatgctg   1006
tcacttaata atcaacctgg ggttcgaaat cagtgagacc tggattcaaa ttctgccttg   1066
aaatattgtg actctgggaa tgacaacacc tggtttgttc tctgttgtat ccccagcccc   1126
aaakwcagct cctggccata tatcaaggtt tcaataaata tttgctaaat gaawaaaaaa   1186
aaaac                                                                1191
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<210> 343
<211> 1070
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 13..465

<221> sig_peptide
<222> 13..75

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<223> Von Heijne matrix
      score 3.9000000953674З
      seq PVAVTAAVAPVLS/IN

<221> polyA_signal
<222> 1035..1040

<221> polyA_site
<222> 1060..1070

<400> 343
agagtcggga aa atg gct gcg agt acc tcc atg gtc ccg gtg gct gtg acg      51
              Met Ala Ala Ser Thr Ser Met Val Pro Val Ala Val Thr
                      -20                 -15                 -10
gcg gca gtg gcg cct gtc ctg tcc ata aac agc gat ttc tca gat ttg        99
Ala Ala Val Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu
             -5                   1               5
cgg gaa att aaa aag caa ctg ctg ctt att gcg ggc ctt acc cgg gag       147
Arg Glu Ile Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu
    10                  15                  20
cgg ggc cta cta cac agt agc aaa tgg tcg gcg gag ttg gct ttc tct       195
Arg Gly Leu Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser
25                  30                  35                  40
ctc cct gca ttg cct ctg gcc gag ctg caa ccg cct ccg cct att aca       243
Leu Pro Ala Leu Pro Leu Ala Glu Leu Gln Pro Pro Pro Pro Ile Thr
                45                  50                  55
gag gaa gat gcc cag gat atg gat gcc tat acc ctg gcc aag gcc tac       291
Glu Glu Asp Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr
            60                  65                  70
ttt gac gtt aaa gag tat gat cgg gca gca cat ttc ctg cat ggc tgc       339
Phe Asp Val Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys
        75                  80                  85
aat gca aga aaa gcc tat ttt ctg tat atg tat tcc aga tat ctg gtg       387
Asn Ala Arg Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val
    90                  95                  100
agg gcc att tta aaa tgt cat tct gcc ttt agt gaa aca tcc ata ttt       435
Arg Ala Ile Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe
105                 110                 115                 120
aga acc aat gga aaa gtt aaa tct ttt aaa tagcttagca gtgggccact         485
Arg Thr Asn Gly Lys Val Lys Ser Phe Lys
                125                 130
gaatgaatgt actttataca tagcaataat aaaaaaaaga tatcataaat aaagttaaaa     545
aggatggtaa aaaaaaaaat attcttagga atgactaaca ggataagtaa caacctgatt     605
atttatttac tttaggttat ataaggttct tcatgcctgt gaattaatat tattgtgtaa     665
gaattaagtt aaaaagcctg ggctgacttt taaatttata aattcattta tcatgtttat     725
agtatattta ttgtttttct ttcatggcta ttaaaaagta tgactgtaaa ggacaatgca     785
agtaaaccaa cttaatactg tattgaataa taagtacaat ttattatttt actttgaaac     845
attatgaatt tactttccta ctttttctta gttgttatct atataaattg attaaaaaaa     905
cattttatgt acttctcatt tcctagtaca ggttgagtat cccttatttg aagtgcttgg     965
gaccaaaagt gtttcagatt tcagattttt ttcagatttt ggtatatttg cattatactt    1025
actggttgaa ataaaaaatg ctgcagtgag tgtcaaaaaa aaaaa                    1070


<210> 344
<211> 1213
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 2..718
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<221> sig_peptide
<222> 2..76
<223> Von Heijne matrix
      score 3.90000009536743
      seq RVGLLLGGGGVYG/SR

<221> polyA_signal
<222> 1170..1175

<221> polyA_site
<222> 1203..1213

<400> 344
a atg ccc cgg aag cgg aag tgc gat ctt cgg gct gtc aga gtt ggt ctg      49
  Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu
  -25                 -20                 -15                 -10
tta ctc ggt ggt ggc gga gtc tac gga agc cgt ttt cgc ttc act ttt        97
Leu Leu Gly Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Phe
                 -5                   1               5
cct ggc tgt aga gcg ctt tcc ccc tgg cgg gtg aga vtg cag aga cga       145
Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg
        10                  15                  20
agg tgc gag atg agc act atg ttc gcg gac act ctc ctc atc gtt ttt       193
Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe
    25                  30                  35
atc tct gtg tgc acg gct ctg ctc gca gag ggc ata acc tgg gtc ctg       241
Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu
40                  45                  50                  55
gtt tac agg aca gac aag tac aag aga ctg aag gca gaa gtg gaa aaa       289
Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys
                60                  65                  70
cag agt aaa aaa ttg gaa aag aag aag gaa aca ata aca gag tca gct       337
Gln Ser Lys Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala
            75                  80                  85
ggt cga caa cag aaa aar aaa ata gag aga cdd kaa kas amc ctg arg       385
Gly Arg Gln Gln Lys Lys Lys Ile Glu Arg Xaa Xaa Xaa Xaa Leu Xaa
        90                  95                 100
aat aac aac aga gat cta tca atg gtt cga atg aaa tcc atg ttt gct       433
Asn Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala
    105                 110                 115
att ggc ttt tgt ttt act gcc cta atg gga atg ttc aat tcc ata ttt       481
Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe
120                 125                 130                 135
gat ggt aga gtg gtg gca aag ctt cct ttt acc cct ctt tct tas rtc       529
Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa
                140                 145                 150
sra gga ctg tct cat cga aat ctg ctg gga gat gac acc aca gac tgt       577
Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys
            155                 160                 165
tcc ttc att ttc ctg taw att ctc tgt act atg tcg att cga cag aac       625
Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn
        170                 175                 180
att cag aag att ctc ggc ctt gcc cct tca cga gcc gcc acc aag cag       673
Ile Gln Lys Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln
    185                 190                 195
gca ggt gga ttt ctt ggc cca cca cct cct tct ggg aag ttc tct           718
Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser
200                 205                 210
tgaactcaag aactctttat tttctakcat tctttctaga cacacacaca tcagactggc    778
aactgttttg tascaagagc cataggtagc cttackactt gggcctcttt ctagttttga    838
attatttcta agccttttgg gtatkattag agtgaaaatg gcagccagca aacttgatag    898
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tgcttttggt cctagatgat ttttatcaaa taagtggatt gattagttaa gttcaggtaa    958
tgtttatgta atgaaaaaca aatagcatcc ttcttgtttc atttacataa gtattttctg   1018
tgggaccgac tctcaaggca ctgtgtatgc cctgcaagtt ggctgtctat gagcatttag   1078
agatttagaa gaaaaattta gtttgtttaa cccttgtaac tgtttgtttt gttgttgttt   1138
tttttcaagg ccaaatacat gacataarat caataaarag gccaaatttt tasctgtttt   1198
atgtaaaaaa aaaaa                                                     1213
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<210> 345
<211> 978
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 86..709

<221> sig_peptide
<222> 86..361
<223> Von Heijne matrix
      score 6.30000019073486
      seq LLMSILALIFIMG/NS

<221> polyA_signal
<222> 943..948

<221> polyA_site
<222> 963..973

<400> 345

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aaagcatcct tccctaggac tgctgtaagc tttgagcctc tagcaggaga catgcctcgg     60
ggacgaaaga gtcggcgccg ccgta atg cga gag ccg cag aag aga acc gca      112
                            Met Arg Glu Pro Gln Lys Arg Thr Ala
                                        -90                 -85

aca atc gca aaa tyc rrg gcs tva gag ggc ctc cga gac ccc tat ggc      160
Thr Ile Ala Lys Xaa Xaa Ala Xaa Glu Gly Leu Arg Asp Pro Tyr Gly
            -80                 -75                 -70

cgc ctc tgt ggt agc gag cac ccc cga aga cca cct gag cgg ccc gag      208
Arg Leu Cys Gly Ser Glu His Pro Arg Arg Pro Pro Glu Arg Pro Glu
        -65                 -60                 -55

gaa gac ccg agc act cca gag gag gcc tct acc acc cct gaa gaa gcc      256
Glu Asp Pro Ser Thr Pro Glu Glu Ala Ser Thr Thr Pro Glu Glu Ala
    -50                 -45                 -40

tcg agc act gcc caa gca caa aag cct tca gtg ccc cgg agc aat ttt      304
Ser Ser Thr Ala Gln Ala Gln Lys Pro Ser Val Pro Arg Ser Asn Phe
-35                 -30                 -25                 -20

cag ggc acc aag aaa agt ctc ctg atg tct ata tta gcg ctc atc ttc      352
Gln Gly Thr Lys Lys Ser Leu Leu Met Ser Ile Leu Ala Leu Ile Phe
                -15                 -10                 -5

atc atg ggc aac agc gcc aag gaa gct ctg gtc tgg aaa gtg ctg ggg      400
Ile Met Gly Asn Ser Ala Lys Glu Ala Leu Val Trp Lys Val Leu Gly
            1               5                   10

aag tta gga atg cag cct gga cgt cas cac agc atc ttt gga gat ccg      448
Lys Leu Gly Met Gln Pro Gly Arg Xaa His Ser Ile Phe Gly Asp Pro
    15                  20                  25

aag aar atc gtc aca gaa ran ttt gtg cgc aga ggg tac ctg att tat      496
Lys Lys Ile Val Thr Glu Xaa Phe Val Arg Arg Gly Tyr Leu Ile Tyr
30                  35                  40                  45

ara ccg gtg ccc cgt abc agt ccg gtg gag tat gas ttc ttc tgg ggg      544
Xaa Pro Val Pro Arg Xaa Ser Pro Val Glu Tyr Xaa Phe Phe Trp Gly
                50                  55                  60
```

```
ccc cga gca cac gtg gaa tcg agc ara ctg aaa stc wtg cat ttt gtg        592
Pro Arg Ala His Val Glu Ser Ser Xaa Leu Lys Xaa Xaa His Phe Val
            65                  70                  75
gca agg gtt cgt aac cga tgc tct aaa gac tgg cct tgt aat tat gac        640
Ala Arg Val Arg Asn Arg Cys Ser Lys Asp Trp Pro Cys Asn Tyr Asp
        80                  85                  90
tgg gat tcg gac gat gat gca gag gtt gag gct atc ctc aat tca ggt        688
Trp Asp Ser Asp Asp Asp Ala Glu Val Glu Ala Ile Leu Asn Ser Gly
    95                  100                 105
gct arg ggt tat tcc gcc cct taagtaratc tgaggcagac ccttgggggt           739
Ala Xaa Gly Tyr Ser Ala Pro
110                 115
gtaaaagaga gtcacaggta ccccaaggag tagatgccag ggtcctaagt tgaaaatgmt      799
gtcgattggg ggcgggggac actgtatttg atatttgtga tcagtgatca ttgttcaact      859
gcgaaataga gtgtttgctt ttgataatgg aaaattgtat tcgttttaaa attccgtttg      919
ttgagaataa caatatgttt aaaaatataa ttgaacaaat tttaaaaaaa aaaamcccy       978
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<210> 346
<211> 810
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 63..320

<221> sig_peptide
<222> 63..179
<223> Von Heijne matrix
score 3.90000009536743
seq VLAIGLLHIVLLS/IP

<221> polyA_signal
<222> 771..776

<221> polyA_site
<222> 799..810

<400> 346

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agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca       60
gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg         107
   Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg
                   -35                 -30                 -25
gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt        155
Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly
                -20                 -15                 -10
ctc ctc cac atc gtg ctg ctg agc atc ccg ttt gtk agt gtc cct gtc        203
Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val
            -5                  1               5
gtc tgg acc ctc acc aac ctc att cac aac atg ggc atg tat atc ttc        251
Val Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe
    10                  15                  20
ctg cac acg gtg aag ggg aca ccc ttt gag acc ccg gac cag ggc aag        299
Leu His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys
25                  30                  35                  40
gcg agg ctg cta acc cac tgg tgagcagatg gattatgggg tccagttcac           350
Ala Arg Leu Leu Thr His Trp
                45
ggcctctcgg aakttcttga ccatcacacc catcgtgctg tacttcctca ccagcttcta      410
cactaaktac raccaaatcc atttgtgct caacaccgtg tccctgatra gcgtgcttat       470
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```
ccccaagctg ccccagctcc acggaktccg gatttttgga atcaataakt actgaaaktg    530
cascccccttc ccctgcccag ggtggcaggg gaggggtagg gtaaaaggca tktgctgcaa    590
chctgaaaac araaaraara rscctctgga cactgccara ratgggggtt gagcctctgg    650
cctaatttcc cccctcgctt cccccagtag ccaacttgga gtagcttgta ytggggttgg    710
ggtaggcccc ctgggctctg acctttctg aatttttga tcttttcctt ttgctttttg    770
aatararact ccatggagtt ggtcatggaa aaaaaaaaa                          810
```

<210> 347
<211> 771
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 299..418

<221> sig_peptide
<222> 299..379
<223> Von Heijne matrix
score 3.59999990463257
seq LTLLLITPSPSPL/LF

<221> polyA_signal
<222> 739..744

<221> polyA_site
<222> 762..771

<400> 347

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accttgggct ccaaattcta gctcataaag atgcaagtkt tgcaatttcc tataaatggt     60
taagaaaaga gcaagctgtc cagagagtga gaagtttgaa aagagaggtg cataagagag    120
aaatgatgtc catttgagcc ccaccacgga ggttatgtgg tcccaaaagg aatgatggcc    180
aagcaattaa tttttcctcc tagttcttag cttgcttctg cattgattgg ctttacacaa    240
ctggcattta gtctgcatta cacaaataga cactaattta tttggaacaa gcagcaaa      298
atg aga act tta ttt ggt gca gtc agg gct cca ttt agt tcc ctc act      346
Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
        -25                 -20                 -15
ctg ctt cta atc acc cct tct ccc agc cct ctt cta ttt gat aga ggt      394
Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
    -10                 -5                  1               5
ctg tcc ctc aga tca gca atg tct tagcccctct cctctcttcc attccttcct     448
Leu Ser Leu Arg Ser Ala Met Ser
                10
gttggtactc atttcttcta acttttaata aacatttagg tataatacat tacagtaagt    508
gctatttaga tacaaactta aaacatacta tatattttaa ggatctaaga atcctttara    568
rrrggcacat gactgaagta cctcagctgc gcagcctgta accagttttt ttaatgtaaa    628
agtaaraatg ccagccttaa cctabccctg carataaaag ctaactttta ttaataccag    688
ccctgaataa tggcactaat ccacactctt ccttaragtg atgctggaaa aataaaatca    748
ggggcttcag attaaaaaaa aaa                                            771
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<210> 348
<211> 409
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 186..380

<221> sig_peptide
<222> 186..233
<223> Von Heijne matrix
score 4
seq FFLFLSFVLMYDG/LR

<221> polyA_signal
<222> 383..388

<221> polyA_site
<222> 396..409

<400> 348
ataaaagaag cagcaaatag aatttcccac aaagtaagtt gactctaaat cttaagtatt 60
acctagtttt ttaaaggttt gaatataata atgcagtatt tgcagtataa aaaggaagga 120
atttgtagag aatcattttg gtgctcaagt ctcttagcag tgccttattg cctcatagca 180
agaag atg ctg ggg ttt ttt ttg ttt ttg tcc ttt gta tta atg tat gat 230
Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp
-15 -10 -5
ggt ttg cgc ctt ttt ggc att ctt tca aca tgt cgt gta cat cac acc 278
Gly Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr
1 5 10 15
atg aat cag ttc cta att gat ata tct agc ttt acc tcc cga gtt aaa 326
Met Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys
20 25 30
aaa aaa atc ttt tta ttt tat gcc ttc awa ggt tgc ycg ttt car agt 374
Lys Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser
35 40 45
gcc aca taaataaaat gtttaacaaa aaaaaaaa 409
Ala Thr

<210> 349
<211> 613
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 69..458

<221> sig_peptide
<222> 69..233
<223> Von Heijne matrix
score 4
seq AALCGISLSQLFP/EP

<221> polyA_signal
<222> 564..569

<221> polyA_site
<222> 602..613

<400> 349
aagaacctga gcagcctgtc ttcagacaga gagaggccca cggctgtttc ttgaaaytgg 60
cgctggga atg gcc atg tgg aac agg cca tgb bag ang ctg cct cag cag 110
Met Ala Met Trp Asn Arg Pro Xaa Xaa Xaa Leu Pro Gln Gln
-55 -50 -45
cct cts sta gct gag ccc act gca gag ggg gag cca cac ctg ccc acg 158
Pro Leu Xaa Ala Glu Pro Thr Ala Glu Gly Glu Pro His Leu Pro Thr

```
    -40                 -35                 -30
ggc cgg gas byg act gag gcc aac cgc ttc gcc tat gct gcc ctc tgt      206
Gly Arg Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu Cys
-25                 -20                 -15                 -10
ggc atc tcc ctg tcc cag tta ttt cct gaa ccc gaa cac agc tcc ttc      254
Gly Ile Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser Phe
                -5                  1               5
tgc aca gag ttc atg gca ggc ctg gtg ckm tgg ctg gag ttg tct gaa      302
Cys Thr Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser Glu
        10                  15                  20
gct gtc ttg cca acc atg act gct ttt gcg agc ggc ctg gga ggt gaa      350
Ala Val Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly Glu
    25                  30                  35
gga sca vma tgt gtt tgt tca aat ttt act gaa gga ccc cat ctt gaa      398
Gly Xaa Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu Glu
40                  45                  50                  55
gga cga ccc gac ggt gat cac tca gga cct tct gag ctt ctc act caa      446
Gly Arg Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr Gln
                60                  65                  70
gga tgg gca cta tgacscccgg gccagagtcc tcgtttgcca catgacctcc          498
Gly Trp Ala Leu
            75
ctgctccaag tgcccttgga ggagctggat gtccttgaaa agatgttcct ggagagcctg    558
aaggaaatca aagaagagga atctgaaatg gccgaggcat cccraaaaaa aaaaa         613
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<210> 350
<211> 986
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 12..638

<221> sig_peptide
<222> 12..263
<223> Von Heijne matrix
score 4.19999980926514
seq ITMLQMLALLGYG/LF

<221> polyA_signal
<222> 951..956

<221> polyA_site
<222> 975..985

<400> 350

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accctatcaa g atg gtc aac ttc ccc cag aaa att gca ggt gaa ctc tat      50
             Met Val Asn Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr
                                     -80                 -75
gga cct ctc atg ctg gtc ttc act ctg gtt gct atc cta ctc cat ggg       98
Gly Pro Leu Met Leu Val Phe Thr Leu Val Ala Ile Leu Leu His Gly
    -70                 -65                 -60
atg aag acg tct gac act att atc cgg gag ggc acc ctg atg ggc aca      146
Met Lys Thr Ser Asp Thr Ile Ile Arg Glu Gly Thr Leu Met Gly Thr
-55                 -50                 -45                 -40
gcc att ggc acc tgc ttc ggc tac tgg ctg gga gtc tca tcc ttc att      194
Ala Ile Gly Thr Cys Phe Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile
                -35                 -30                 -25
tac ttc ctt gcc tac ctg tgc aac gcc cag atc acc atg ctg cag atg      242
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```
Tyr Phe Leu Ala Tyr Leu Cys Asn Ala Gln Ile Thr Met Leu Gln Met
            -20                 -15                 -10
ttg gca ctg ctg ggc tat ggc ctc ttt ggg cat tgc att gtc ctg ttc      290
Leu Ala Leu Leu Gly Tyr Gly Leu Phe Gly His Cys Ile Val Leu Phe
        -5                  1               5
atc acc tat aat atc cac ctc cgc gcc ctc ttc tac ctc ttc tgg ctg      338
Ile Thr Tyr Asn Ile His Leu Arg Ala Leu Phe Tyr Leu Phe Trp Leu
10                  15                  20                  25
ttg gtg ggt gga ctg tcc aca ctg cgc atg gta gca gtg ttg gtg tct      386
Leu Val Gly Gly Leu Ser Thr Leu Arg Met Val Ala Val Leu Val Ser
                30                  35                  40
cgg acc gtg ggc ccc aca cad cgg mtg ctc ctc tgt ggc acc ctg gct      434
Arg Thr Val Gly Pro Thr Xaa Arg Xaa Leu Leu Cys Gly Thr Leu Ala
            45                  50                  55
gcc cta cac atg ctc ttc ctg ctc tat ctg cat ttt gcc tac cac aaa      482
Ala Leu His Met Leu Phe Leu Leu Tyr Leu His Phe Ala Tyr His Lys
        60                  65                  70
dtg gta dag ggg atc ctg gac aca ctg gag ggc ccc aac atc ccg ccc      530
Xaa Val Xaa Gly Ile Leu Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro
    75                  80                  85
atc cag agg gtc ccc aga gac atc cct gcc atg ctc cct gct gct cgg      578
Ile Gln Arg Val Pro Arg Asp Ile Pro Ala Met Leu Pro Ala Ala Arg
90                  95                  100                 105
ctt ccc acc acc gtc ctc aac gcc aca gcc aaa gct gtt gcg gtg acc      626
Leu Pro Thr Thr Val Leu Asn Ala Thr Ala Lys Ala Val Ala Val Thr
                110                 115                 120
ctg cag tca cac tgaccccacc tgaaattctt ggccagtcct ctttcccgca          678
Leu Gln Ser His
            125
gctgcagaga ggargaasac tattaaagga cagtcctgat gacatgtttc gtagatgggg    738
tttgcagctg ccactgagct gtagctgcgt aagtacctcc ttgatgcctg tcggcacttc    798
tgaaaggcac aaggccaaga actcctggcc aggactgcaa ggctctgcag ccaatgcaga    858
aaatgggtca gctcctttga gaacccctcc ccacctaccc cttccttcct ctttatctct    918
cccacattgt cttgctaaat atagacttgg taattaaaat gttgattgaa gtctggaaaa    978
aaaaaaat                                                             986
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<210> 351
<211> 1447
<212> DNA
<213> Homo sapiens

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<221> CDS
<222> 282..389

<221> sig_peptide
<222> 282..332
<223> Von Heijne matrix
      score 3.5
      seq RWWCFHLQAEASA/HP

<221> polyA_signal
<222> 1413..1418

<221> polyA_site
<222> 1437..1447

<400> 351
ataataatat ctaaaaagct aaattttaaa taccagcttt acataaatga ttgtkgactc     60
tggtctgtkt ctgacacctt tccagaaaaa agtcaattgt tcaggtacac caaagaggaa    120
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gaagagctgt ggaggccacc ctctacaaag ctttatagaa cttctggatc taactcacaa    180
acaagcttcc agaagagact agagacctta ggccaggaga tgaaggagtt cagtagcaaa    240
gtcacacctg tccaattccc tgagctttgc tcactcagct a atg gga tgg caa agg    296
                                              Met Gly Trp Gln Arg
                                                      -15
tgg tgg tgc ttt cat ctt cag gca gaa gcc tct gcc cat ccc cct caa      344
Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser Ala His Pro Pro Gln
        -10                 -5                  1
ggg ctg cag gcc caa ttc tca tgc tgc cct tgg gtg ggc atc tgt          389
Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp Val Gly Ile Cys
5                   10                  15
taacaaadga aaacgtctgg gtggcggcag cascttttgct ctgagtgcct acaaagctaa   449
tgcttggtgc tagaaacatc atcattatta aacttcagaa aagcagcagc catgttcagt    509
caggctcatg ctgcctcact gcttaagtgc ctgcaggagc cgcctgccaa rctccccttc    569
ctacacctgg cacactgggg tctgcacaag gctttgtcaa ccaaaracag cttcccccww    629
ttgattgcct gtagactttg gagccaaraa acactctgtg tgactctaca cacacttcag    689
gtggtttgtg cttcaaagtc attgatgcaa cttgaaagga aacagtttaa tggtggaaat    749
gaactaccat ttataacttc tgttttttta ttgagaaaat gattcacgaa kkccaaatca    809
gattgccagg aagaaatagg acgtgacggt actgggccct gtgattctcc cagcccttgc    869
agtccgctag gtgagaggaa aagctcttta cttccgcccc tggcagggac ttctgggtta    929
tgggagaaac cagagatggg aatgaggaaa atatgaacta cagcagaagc ccctgggcag    989
ctgtgatgga gcccctgaca ttactcttct tgcatctgtc ctgccttctt tccctctgcg   1049
aggcagtggg gtgggattca gagtgcttag tctgctcact gggagaagaa gagttcctgc   1109
gcatgcaagc cctgctgtgt ggctgtcgtt tacatttggg aggtgtcctg tatgtctgta   1169
cgttggggac tgcctgtatt tggaagattt aaaaacctag catcctgttc tcaccctcta   1229
agctgcattg agaaatgact cgtctctgta tttgtattaa gccttaacac ttttcttaag   1289
tgcattcggt gccaacattt tttagagctg taccaaaaca aaaagcctgt actcacatca   1349
camtgtcatt ttgataggag cgttttgtta tttttacaag gcagaatggg gtgtaacagt   1409
tgaattaaac ttagcaatca cgtgctcaaa aaaaaaa                             1447
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<210> 352
<211> 1641
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 208..339

<221> sig_peptide
<222> 208..294
<223> Von Heijne matrix
score 5.59999990463257
seq LFLQLLVSHEIVC/AT

<221> polyA_site
<222> 1631..1641

<400> 352

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agaaccgtga tgggaagatg gacaaggaag agaccaaaga ctggatcctt ccctcagact     60
atgatcatgc agaggcagaa gccaggcacc tggtctatga atcagaccaa aacaaggatg    120
gcaagcttac caaggaggag atcgttgaca agtatgactt atttgttggc agccaggcca    180
cagattttgg ggaggcctta gtacggc atg atg agt tct gag cta cgg agg aac    234
                              Met Met Ser Ser Glu Leu Arg Arg Asn
                                              -25
cct cat ttc ctc aaa agt aat tta ttt tta cag ctt ctg gtt tca cat      282
Pro His Phe Leu Lys Ser Asn Leu Phe Leu Gln Leu Leu Val Ser His
-20                 -15                 -10                 -5
gaa att gtt tgc gct act gag act gtt act aca aac ttt tta aga cat      330
Glu Ile Val Cys Ala Thr Glu Thr Val Thr Thr Asn Phe Leu Arg His
```

```
                                   1                 5                   10
gaa aag gcg taatgaaaac catcccgtcc ccattcctcc tcctctctga        379
Glu Lys Ala
        15
gggactggag ggaagccgtg cttctgagga acaactctaa ttagtacact tgtgtttgta   439
ratttacacw wtgtattatg tattaacatg gcgtgtttat ttttgtattt ttctctggtt   499
gggagtatka tatgaaggat caaratcctc aactcacaca tgtaracaaa cattasctct   559
ttactctttc tcaacccctt wtatgatttt aataattctc acttaactaa ttttgtaagc   619
ctgagatcaa taagaaatgt tcaggagaga ggaaagaaaa aaaatatatg ctccacaatt   679
tatatttaga gagagaacac ttagtcttgc ctgtcaaaaa gtccaacatt tcataggtag   739
taggggccac atattacatt cagttgctat aggtccagca actgaacctg ccattacctg   799
ggcaaggaaa gatccctttg ctctaggaaa gcttggccca aattgatttt cttctttttc   859
cccctgtagg actgactgtt ggctaatttt gtcaagcaca gctgtggtgg gaagagttag   919
ggccagtgtc ttgaaaatca atcaagtagt gaatgtgatc tctttgcara gctatagata   979
gaaacagctg gaaaactaaa ggaaaaatac aagtgtttc ggggcataca tttttttct    1039
gggtgtgcat ctgttgaaat gctcaagact taattatttg ccttttgaaa tcactgtaaa  1099
tgcccccatc cggttcctct tcttcccarg tgtgccaagg aattaatctt ggtttcacta  1159
caattaaaat tcactccttt ccaatcatgt cattgaaagt gcctttaacg aaagaaatgg  1219
tcactgaatg ggaattctct taagaaaccc tgagattaaa aaaagactat ttggataact  1279
tataggaaag cctagaacct cccagtagag tggggatttt tttcttcttc cctttctctt  1339
ttggacaata gttaaattag cagtattagt tatgagtttg gttgcagtgt tcttatcttg  1399
tgggctgatt tccaaaaacc acatgctgct gaatttacca gggatcctca tacctcacaa  1459
tgcaaaccac ttactaccag gccttttctt gtgtccactg gagagcttga gctcacactc  1519
aaagatcaga ggacctacag agagggctct ttggtttgag gaccatggct tacctttcct  1579
gcctttgacc catcacaccc catttcctcc tctttccctc tccccgctgc caaaaaaaaa  1639
aa                                                                 1641
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<210> 353
<211> 884
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 69..557

<221> sig_peptide
<222> 69..224
<223> Von Heijne matrix
score 4.69999980926514
seq LGLALGRLEGGSA/RH

<221> polyA_signal
<222> 849..854

<221> polyA_site
<222> 870..883

<400> 353

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attggctccg gatcgtgcgt gaggcggctt cgtgggcagc gagagtcaca gacaagacag    60
caagcagg atg gag cac tac cgg aaa gct ggc tct gta gag ctc cca gcg     110
         Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro Ala
                 -50                 -45                 -40
cct tcc cca atg ccc cag cta cct cct gat acc ctt gag atg cgg gtc     158
Pro Ser Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg Val
            -35                 -30                 -25
cga gat ggc agc aaa att cgc aac ctg ctg ggg ttg gct ctg ggt cgg     206
Arg Asp Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly Arg
        -20                 -15                 -10
ttg gag ggc ggc agt gct cgg cat gta gtg ttc tca ggt tct ggc agg     254
```

```
Leu Glu Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg
    -5                  1               5                   10
gct gca gga aag gct gtc agc tgc gct gag att gtc aag cgg cgg gtc     302
Ala Ala Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val
            15                  20                  25
ccg ggc ctg cac cag ctc acc aag cta ckt ttc ctt caa act gag gac     350
Pro Gly Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp
            30                  35                  40
agc tgg gtc cca scc tca cct gac aca ggg cta rac ccc ctc aca gtg     398
Ser Trp Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val
        45                  50                  55
cgc cgc cat gtg cct gca ktg tgg gtg ctg ctc asc cgg gac ccc ctg     446
Arg Arg His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu
    60                  65                  70
gac ccc aat gag tgt ggt tac caa ccc cca gga gca ccc cct ggc ctg     494
Asp Pro Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu
75                  80                  85                  90
ggt tcc atg ccc agc tcc agc tgt ggc cct cgt tcc cra aaa agg gct     542
Gly Ser Met Pro Ser Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala
                95                  100                 105
cra rac acc cga tcg tgaaaacctg ctgasccagc ctgttctccg ggcctraatg     597
Xaa Xaa Thr Arg Ser
            110
tctggggtgc ttgtgccttt tctranaagc gttgtgaskg ctcaacatcc ccatcaaggt   657
ttgagtccac aaaagtggac ctccctatca tgcttcccct tccctctagc atgtgggaag   717
ggactgctgt gaagaatgac agatgtgggg cctctgccaa gttctgcatt gctaaataag   777
ggcttcctct gccttctacc tacagtgcat ttgaactgcc ttctgaaaga ggtccakgga   837
gggatttagg aaataaagtt tctacctatt tgaaaaaaaa aaaacac                 884
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&lt;210&gt; 354
&lt;211&gt; 729
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; CDS
&lt;222&gt; 134..325

&lt;221&gt; sig_peptide
&lt;222&gt; 134..274
&lt;223&gt; Von Heijne matrix
      score 5.90000009536743
      seq TWLGLLSFQNLHC/FP

&lt;221&gt; polyA_site
&lt;222&gt; 718..729

&lt;400&gt; 354
atcattttct tatccctgct gatttcaaac cttcccatgg tttagaagca taacctgtaa    60
tgtaatgcaa gtcccctaac tccctggttg ctaacattaa cttccttaag taataatcaa   120
tgaaagavat tct atg cat ggt ttt gaa ata ata tcc ttg aaa gag gaa      169
               Met His Gly Phe Glu Ile Ile Ser Leu Lys Glu Glu
                           -45                 -40
tca cca tta gga aag gtg agt cag ggt cct ttg ttt aat gtg act agt     217
Ser Pro Leu Gly Lys Val Ser Gln Gly Pro Leu Phe Asn Val Thr Ser
-35                 -30                 -25                 -20
ggc tca tca tca cca gtg acc tgg ttg ggc cta ctc tcc ttc cag aac     265
Gly Ser Ser Ser Pro Val Thr Trp Leu Gly Leu Leu Ser Phe Gln Asn
                -15                 -10                 -5
ctg cat tgc ttc cca gac ctc ccc act gag atg cct cta ara gcc aaa     313
```

```
Leu His Cys Phe Pro Asp Leu Pro Thr Glu Met Pro Leu Xaa Ala Lys
            1               5                   10
gga ktc aac act tgagcctagg gtgggctaca acaaaaratt ctaatttacc       365
Gly Xaa Asn Thr
    15
ttgcttcatc taggtccagg ccccaaktag cttgctgaag gaacttaaaa agtagctgtt 425
atttattgta ttgtataasc taaaaacatt tatttttgtt gaatcraaac aattccatgt 485
ascaatcttt tttctgttca cggtgtttgt gataaaacct taaattccgc aagcatcagt 545
tttttgaaaa aatgggaatt gaccggatag wwacaggcaa agwtataaat agctacaaca 605
tcatttaact tttataaaca tgccttctct ctattgaara catctgatat ttttgctgga 665
aagttggatc tatcctcagt aactctgcca tgaattcctg tttcckggtt ccaaaaaaaa 725
aaaa                                                              729


<210> 355
<211> 1013
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 78..731

<221> sig_peptide
<222> 78..227
<223> Von Heijne matrix
      score 5.09999990463257
      seq RTALILAVCCGSA/SI

<221> polyA_site
<222> 1002..1013

<400> 355
agtttccaag ggaaggagca gcgtgtggga aagcacagaa gagtgagaag gaagcgacta  60
aattttattt actttct atg cat cat ggc ctc aca cca ctg tta ctt ggt    110
                   Met His His Gly Leu Thr Pro Leu Leu Leu Gly
                   -50                 -45                 -40
gta cat gag caa aaa cag caa gtg gtg aaa ttt tta atc aag aaa aaa   158
Val His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys
                -35                 -30                 -25
gca aat tta aat gca ctg gat aga tat gga aga act gct ctc ata ctt   206
Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu
            -20                 -15                 -10
gct gta tgt tgt gga tcg gca agt ata gtc agc ctt cta ctt gag caa   254
Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln
        -5                  1               5
aac att gat gta tct tct caa gat cta tct gga cag acg gcc aaa aag   302
Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Lys Lys
10                  15                  20                  25
tat gct gtt tct agt cgt cat aat gta att tgc cag tta ctt tct gac   350
Tyr Ala Val Ser Ser Arg His Asn Val Ile Cys Gln Leu Leu Ser Asp
                30                  35                  40
tac aaa raa aaa cag atr cta aaa gtc tct tct gaa aac agc aat cca   398
Tyr Lys Xaa Lys Gln Xaa Leu Lys Val Ser Ser Glu Asn Ser Asn Pro
            45                  50                  55
raa caa gac tta aag ctg aca tca gag gaa gag tca caa agg ctt aaa   446
Xaa Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Lys
        60                  65                  70
gga agt gaa aat agc cag cca gag gaa atg tct caa gaa cca gaa ata   494
Gly Ser Glu Asn Ser Gln Pro Glu Glu Met Ser Gln Glu Pro Glu Ile
    75                  80                  85
```

aat arg ggt ggt gat aga aag gtt gaa raa raa atg aar aag cac gga 542
Asn Xaa Gly Gly Asp Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly
90 95 100 105
agt wct cat atg gga ttc cca raa aac ctg mct aac ggt gcc act gct 590
Ser Xaa His Met Gly Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala
110 115 120
gac aat ggt gat gat gga tta att ccm cca rgg aaa asc ara aca cct 638
Asp Asn Gly Asp Asp Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro
125 130 135
gaa agc cas caa ttt cct gac act gag aat gaa cag tat cac agg gac 686
Glu Ser Xaa Gln Phe Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp
140 145 150
ttt tct ggc cat ccc mac ttt ccc acd acc ctt ccc atc aaa cag 731
Phe Ser Gly His Pro Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln
155 160 165
tgatgaacaa aatgatactc hsaagcmmct ttctgaagam caraacactg gaatattaca 791
agatgagatt ctgattcatg aagaaaagca gatagaagtg gctgaaaatg aattctgagc 851
tttctcttag ttataaraaa gaaaaagacc tcttgcatga aaatagtacg ttgcaggaag 911
aaattgtcat gctaaractg gaactagack taatgaaaca tcagagccag ctaararaaa 971
araaatattt ggaggaaatt gaaagtgtgg aaaaaaaaaa aa 1013

<210> 356
<211> 973
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..693

<221> sig_peptide
<222> 46..90
<223> Von Heijne matrix
score 7.59999990463257
seq CVLVLAAAAGAVA/VF

<221> polyA_signal
<222> 937..942

<221> polyA_site
<222> 962..973

<400> 356
aagcggctgg tccccggaag ttggacgcat gcgccgtttc tctgc atg gtg tgc gtt 57
Met Val Cys Val
-15
ctc gtt cta gct gcg gcc gca gga gct gtg gcg gtt ttc cta atc ctg 105
Leu Val Leu Ala Ala Ala Ala Gly Ala Val Ala Val Phe Leu Ile Leu
-10 -5 1 5
cga ata tgg gta gtg ctt cgt tcc atg gac gtt acg ccc cgg gag tct 153
Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr Pro Arg Glu Ser
10 15 20
ctc agt atc ttg gta gtg gct ggg tcc ggt ggg cat acc act gag atc 201
Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His Thr Thr Glu Ile
25 30 35
ctg agg ctg ctt ggg agc ttg tcc aat gcc tac tca cct aga cat tat 249
Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser Pro Arg His Tyr
40 45 50
gtc att gct gac act gat gaa atg agt gcc aat aaa ata aat tct ttt 297
Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys Ile Asn Ser Phe

```
    55                  60                  65
gaa cta rat cga gsk gat aga rac cct agt aac atg twt acc aaa tac      345
Glu Leu Xaa Arg Xaa Asp Arg Xaa Pro Ser Asn Met Xaa Thr Lys Tyr
70                  75                  80                  85
tac att cac cga att cca ara agc cgg gag gtt cag cag tcc tgg ccc      393
Tyr Ile His Arg Ile Pro Xaa Ser Arg Glu Val Gln Gln Ser Trp Pro
                90                  95                  100
tcc acc gtt tyc acc acc ttg cac tcc atg tgg ctc tcc ttk ccc cta      441
Ser Thr Val Xaa Thr Thr Leu His Ser Met Trp Leu Ser Xaa Pro Leu
            105                 110                 115
att cac agg gtg aag cca rat ttg gtg ttg tgt aac gga cca gga aca      489
Ile His Arg Val Lys Pro Xaa Leu Val Leu Cys Asn Gly Pro Gly Thr
        120                 125                 130
tgt gty cct atc tgt gta tct gcc ctt ctc ctt ggg ata cta gga ata      537
Cys Val Pro Ile Cys Val Ser Ala Leu Leu Leu Gly Ile Leu Gly Ile
    135                 140                 145
aag aaa gtg atc att gtc tac gtt gaa agc atc tgc cgt gta aaa acs      585
Lys Lys Val Ile Ile Val Tyr Val Glu Ser Ile Cys Arg Val Lys Thr
150                 155                 160                 165
tta tcc atg tcc gga aag att ctg ttt cat ctc tca aat tac ttc att      633
Leu Ser Met Ser Gly Lys Ile Leu Phe His Leu Ser Asn Tyr Phe Ile
                170                 175                 180
gtt cag tgg ccg gct ctg aaa gaa aag tat ccc aaa tcg gtg tac ctt      681
Val Gln Trp Pro Ala Leu Lys Glu Lys Tyr Pro Lys Ser Val Tyr Leu
            185                 190                 195
ggg cga att gtt tgacaaatgg caactgactt ctttagaatt ttgcasttaa          733
Gly Arg Ile Val
        200
cagtartatg tactcaaatt gggggraaaa aaaccctaca tgtttcttgt aaaggcgtct    793
gacagtcctg araattattg atggtaagga ataaaaaatg twcagatrac tcagtgaara    853
aactgaggct tctcttatga aacaaacatt gataaacgta actacyaaat gtttatgcct    913
ctgtaaacca aatttctttt ctarataaaa atatgtatta ctacctgcaa aaaaaaaaaa    973
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<210> 357
<211> 868
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 126..527

<221> sig_peptide
<222> 126..182
<223> Von Heijne matrix
score 3.90000009536743
seq ILFHGVFYAGGFA/IV

<221> polyA_signal
<222> 834..839

<221> polyA_site
<222> 856..867

<400> 357

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actggaagaa ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt     60
gcctttgatg attttcaaga gagttgtgct atgatgtggc aaagtatgca ggaagcaggc    120
ggtca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc    170
      Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala
                  -15                 -10                 -5
```

```
ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg      218
Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg
                1           5                   10
act tta tat tac aag ttg gca gtg gar cag ctg car arc cat ccc gag      266
Thr Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Xaa His Pro Glu
        15                  20                  25
gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc      314
Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu
    30                  35                  40
atc gac agg gaa aac ttc gtg gac att gtt rat gcc aag ttg aaa att      362
Ile Asp Arg Glu Asn Phe Val Asp Ile Val Xaa Ala Lys Leu Lys Ile
45                  50                  55                  60
cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc      410
Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser
                65                  70                  75
aga ggt ggc ccc ttt cag agg tgg cac ctt gac gag gtc ttt tta gag      458
Arg Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu
            80                  85                  90
ctc aag gat ggt cag cag att cct gtg ttc aag ctc agt ggg gaa aac      506
Leu Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn
        95                  100                 105
ggt gat gaa gtg aaa aag gag tagagacgac ccagaagacc cagcttgctt        557
Gly Asp Glu Val Lys Lys Glu
    110                 115
ctagtccatc cttccctcat ctctaccata tggccactgg ggtggtggcc catctcagtg    617
acagacactc ctgcaaccca gktttccagc caccagtggg atgatggtat gtgccagcac    677
atggtaattt tggtgtaatt ctaacttggg cacaacgaat gctatttgtc atttttaaac    737
tgaatccgaa agaaactcct attataaatt taagataatg taatgtattt gaaagtgctt    797
tgtataaaaa agcacatgat aaaaggaatc agaattaata aaatgtttgt tgatctttaa    857
aaaaaaaaaa h                                                         868
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<210> 358
<211> 519
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 66..320

<221> sig_peptide
<222> 66..113
<223> Von Heijne matrix
score 3.5
seq TALAAXTWLGVWG/VR

<221> polyA_signal
<222> 490..495

<221> polyA_site
<222> 508..519

<400> 358

```
aattagcgcg taacgcasag actgcttgct gcggcagaga cgccagakgt gcagctccag    60
cagca atg gca gtg acg gcg ttg gcg gcg mrg acg tgg ctt ggc gtg tgg   110
      Met Ala Val Thr Ala Leu Ala Ala Xaa Thr Trp Leu Gly Val Trp
          -15                 -10                 -5
ggc gtg agg acc atg caa gcc cga ggc ttc ggc tcg gat cag tcc gag      158
Gly Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu
    1               5                   10                  15
```

```
aat gtc gac cgg ggc gcg ggc tcc atc cgg gaa gcc ggt ggg gcc ttc      206
Asn Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe
                20                  25                  30
gga aag aga gag cag gct gaa gag gaa cga tat ttc cga gca cag agt      254
Gly Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg Ala Gln Ser
            35                  40                  45
aca gaa caa ctg gca rct ttg aaa aaa crc cat gaa gaa gar atc gtt      302
Thr Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Ile Val
        50                  55                  60
cat cat aga gaa gga gat tgagcgtctg cagaaagaaa ttgagcgcca             350
His His Arg Glu Gly Asp
    65
taagcagaag atcaaaatgc tagaacatga tgattaagtg cacaccgtgt gccatagaat    410
ggcacatgtc attgcccact tctgtgtaaa catggttctg gtttaactaa tatttgtctg    470
tgtgctacta acagattata ataaattgtc atcagtgaaa aaaaaaaaa                519
```

```
<210> 359
<211> 1028
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 73..948

<221> sig_peptide
<222> 73..159
<223> Von Heijne matrix
      score 4.40000009536743
      seq IVLHLVLQGMVYT/EY

<221> polyA_site
<222> 1016..1028

<400> 359
agctttaaag gcctggccag gggaggagca cagatatttt cctgtataat tccagaatgt     60
cttcagagag cc atg cat gga ttg ctt cat tac ctt ttc cat acg aga aac    111
              Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn
                          -25                 -20
cac acc ttc att gtc ctg cac ctg gtc ttg caa ggg atg gtt tat act      159
His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr
    -15                 -10                  -5
gag tac acc tgg gaa gta ttt ggc tac tgt cag gag ctg gag ttg tcc      207
Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser
1               5                   10                  15
ttg cat tac ctt ctt ctg ccc tat ctg ctg cta ggt gta aac ctg ttt      255
Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu Phe
            20                  25                  30
ttt ttc acc ctg act tgt gga acc aat cct ggc att ata aca aaa gca      303
Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala
        35                  40                  45
aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt      351
Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe
    50                  55                  60
cca aaa aac gtg agg tgc tct act tgt gat tta agg aaa cca gct cga      399
Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg
65                  70                  75                  80
tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat      447
Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His
                85                  90                  95
```

```
cac tgt gtt tgg gtg aac aac tgc atc ggg gcc tgg aac atc agg tmc      495
His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg Xaa
            100                 105                 110
ttc ctc atc tac gtc ttg acc ttg acg gcc tcg gct gcc acc gtc gcc      543
Phe Leu Ile Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val Ala
        115                 120                 125
att gtg agc acc act ttt ctg gtc cac ttg gtg gtg atg tca gat tta      591
Ile Val Ser Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp Leu
    130                 135                 140
tac cag gag act tac atc gat gac ctt gga cac ctc cat gtt atg gac      639
Tyr Gln Glu Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met Asp
145                 150                 155                 160
acg gtc ttt ctt att cag tac ctg ttc ctg act ttt cca cgg att gtc      687
Thr Val Phe Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile Val
                165                 170                 175
ttc atg ctg ggc ttt gtc gtg gtt ctg arc ttc ctc ctg ggt ggc tac      735
Phe Met Leu Gly Phe Val Val Val Leu Xaa Phe Leu Leu Gly Gly Tyr
            180                 185                 190
ctg ttg ttt gtc ctg tat ctg gcg gcc acc aac cag act act aac gag      783
Leu Leu Phe Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn Glu
        195                 200                 205
tgg tac aga rgt gac tgg gcc tgg tgc cag cgt tgt ccc ctt gtg gcc      831
Trp Tyr Arg Xaa Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val Ala
    210                 215                 220
tgg cct ccg tca gca gar ccc caa gtc cac cgg aac att cac tcc cat      879
Trp Pro Pro Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser His
225                 230                 235                 240
ggg ctt cgg arc aac ctt caa gar atc ttt cta cct gcc ttt cca tgt      927
Gly Leu Arg Xaa Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro Cys
                245                 250                 255
cat gag agg aag aaa caa gaa tgacmagtgt atgactgcct ttgagctgta         978
His Glu Arg Lys Lys Gln Glu
            260
gttcccgttt atttacacat gtggatcctc gttttccaaa aaaaaaaaa                1028
```

<210> 360
<211> 452
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 69..434

<221> sig_peptide
<222> 69..236
<223> Von Heijne matrix
score 4.90000009536743
seq FACVPGASPTTLA/FP

<221> polyA_signal
<222> 419..424

<221> polyA_site
<222> 441..452

<400> 360

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acagcgtgas tcgcccgcca gaagaatatg aaaaagcaga gcganctcgg ttaagggaaa     60
gcgccgag atg acg ggc ttt ctg ctg ccg ccc gca agc aga ggg act cgg     110
         Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg
```

```
            -55                 -50                 -45
aga tca tgc agc aga agc aga aaa agg caa acg aga aga agg agg aac      158
Arg Ser Cys Ser Arg Ser Arg Lys Arg Gln Thr Arg Arg Arg Arg Asn
        -40                 -35                 -30
cca agt agc ttt gtg gct tcg tgt cca acc ctc ttg ccc ttc gcc tgt      206
Pro Ser Ser Phe Val Ala Ser Cys Pro Thr Leu Leu Pro Phe Ala Cys
    -25                 -20                 -15
gtg cct gga gcc agt ccc acc acg ctc gcg ttt cct cct gta ktg ctc      254
Val Pro Gly Ala Ser Pro Thr Thr Leu Ala Phe Pro Pro Val Xaa Leu
-10                 -5                  1                   5
aca ggt ccc avc acc gat ggc att ccc ttt gcc ctr nak tct gca gcg      302
Thr Gly Pro Xaa Thr Asp Gly Ile Pro Phe Ala Leu Xaa Ser Ala Ala
            10                  15                  20
ggt ccc ttt tgt gct tcc ttc ccc tca ggt avc ctc tct ccc cct ggg      350
Gly Pro Phe Cys Ala Ser Phe Pro Ser Gly Xaa Leu Ser Pro Pro Gly
        25                  30                  35
cca ctc ccg ggg gtg agg ggg tta ccc ctt ccc agt gtt ttt tat tcc      398
Pro Leu Pro Gly Val Arg Gly Leu Pro Leu Pro Ser Val Phe Tyr Ser
    40                  45                  50
tgt ggg gct cac ccc aaa gta tta aaa gta gct ttg taattcaaaa           444
Cys Gly Ala His Pro Lys Val Leu Lys Val Ala Leu
55                  60                  65
aaaaaaa                                                              452
```

<210> 361
<211> 875
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 628..804

<221> sig_peptide
<222> 628..711
<223> Von Heijne matrix
score 4.19999980926514
seq LMPVIPALQEAXA/GG

<221> polyA_site
<222> 864..875

<400> 361

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aaagatggac accgcggagg aagacatatg tagagtgtgt cggtcagaag gaacacctga     60
gaaaccgctt tatcatcctt gtgtatgtac tggcagtatt aagttngtcc atcaagaatg    120
cttagttcaa tggctgaaac acagtcgaaa agaatactgt gaattatgca agcacagatt    180
tgcttttaca ccaatttatt ctccagatat gccttcacgg cttccaattc aagacatatt    240
tgctggactg gttacaagta ttggcactgc aatacgatat tggtttcatt atacacttgt    300
ggcctttgca tggttgggag ttgttcctct tacagcatgt gagtattcat gcctctgatt    360
ggagttattt aaacattgca taactactta atattataaa gcaatattgc atcatattat    420
tatttgactg atgtttagtt atttgatgtc agagtgtcat gtattaggaa agccttactt    480
araaratgtt catcggaact aaraatgakt ttaacaggtc agttttttga gtgaatgtgg    540
gaaaraacac agcatacaga atggctaacc atgaaagttc atgaaagcgt kgaaaaaatc    600
aaatcaaatc ataattagat atgaagt atg cta rag ctt tca agg gct aca aaa    654
                              Met Leu Xaa Leu Ser Arg Ala Thr Lys
                                              -25                 -20
rac ggc cgg gcg cgg tgg ctt atg cct gta atc cca gca ctt cag gag      702
Xaa Gly Arg Ala Arg Trp Leu Met Pro Val Ile Pro Ala Leu Gln Glu
            -15                 -10                 -5
gcc gan gca ggc gga tca cga ggt cag gag ttt gaa act agc ctg gcc      750
```

```
Ala Xaa Ala Gly Gly Ser Arg Gly Gln Glu Phe Glu Thr Ser Leu Ala
            1               5                  10
aac atg gag act gag gca gga gaa ttg ctt aaa ccc agg agg cgg agg        798
Asn Met Glu Thr Glu Ala Gly Glu Leu Leu Lys Pro Arg Arg Arg Arg
    15                  20                  25
ttg car tgaactgaga tcgcaccact gcactccagc ttgggcaaca gagcaagact         854
Leu Gln
30
ttgtctcgca aaaaaaaaaa a                                                875
```

<210> 362
<211> 531
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 70..366

<221> sig_peptide
<222> 70..108
<223> Von Heijne matrix
score 3.5
seq MHLLSNWANPASS/RR

<221> polyA_signal
<222> 496..501

<221> polyA_site
<222> 521..531

<400> 362

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aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg       60
cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga     111
          Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg
                      -10                 -5                  1
cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc      159
Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu
            5                   10                  15
gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc      207
Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys
        20                  25                  30
tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac      255
Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn
    35                  40                  45
agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca      303
Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr
50                  55                  60                  65
cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt      351
Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu
                70                  75                  80
ttg gga cgc caa ttg taaktgttac cttcaaagga tttccttttc taaaaaatta      406
Leu Gly Arg Gln Leu
            85
ttttaratgt ctaactttat gttattgctc acgggtattt gactgaattg ttgatttagg    466
ataagtcaat tcctggaggg aaattaccaa ataaaatgat atgtatttct taccacaaaa    526
aaaaa                                                                 531
```

<210> 363
<211> 1244
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 70..366

<221> sig_peptide
<222> 70..108
<223> Von Heijne matrix
score 3.5
seq MHLLSNWANPASS/RR

<221> polyA_site
<222> 1233..1244

<400> 363
aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg 60
cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga 111
Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg
-10 -5 1
cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc 159
Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu
5 10 15
gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc 207
Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys
20 25 30
tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac 255
Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn
35 40 45
agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca 303
Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr
50 55 60 65
cca atg aga aga tct tca tgc cat tta raa tgt cag gtt ata ttc ctt 351
Pro Met Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu
70 75 80
ttg gga cgc caa ttg tagtcggtct tctcttgccc aaccagacac tggcatccac 406
Leu Gly Arg Gln Leu
85
tgtcttctgg cagtggctga accagagcca caatgcctgt gtcaactatg caaaccgcaa 466
tgcraccaag ccttcacctg catccaagtt catccaggga tacctgggag ctgtcatcag 526
cgccgtctcc attgctgtgg gccttatktc ctggttcaga aagccaacaa gttcacccca 586
gccacccgcc ttctcatcca gaggtttgtg ccgttccctg ctgtagccag tgccaatatc 646
tgcaatgtgg tcctgatgcg gtacggggag ctggaggaag ggattgatgt cctggacagc 706
gatggcaacc tcgtgggctc ctccaagatc gcagcccgac acgccctgct ggagacggcg 766
ctgacgcgag tggtcctgcc catgcccatc ctggtgctac cccgatcgt catgtccatg 826
ctggagaaga cggctctcct gcaggcacgc ccccggctgc tcctccctgt gcaaagcctc 886
gtgtgcctgg cagccttcgg cctggccctg ccgctggcca tcagcctctt cccgcaaatg 946
tcagagattg aaacatccca attagagccg gagatagccc aggccacgag cagccggaca 1006
gtggtgtaca acaaggggtt gtgagtgtgg tcagcggcct ggggacggag cactgtgcag 1066
ccggggagct gaggggcarg gccgtagact cacggctgca cctgcaggga gcagcacgcc 1126
aaccccagca gtcctgggcc ccctgggaga gtgctcaacc tacagtggag ggagactgac 1186
ccattcacat tttaacatag gcaagaggag ttctaacaca tttcgtacaa aaaaaaaa 1244

<210> 364
<211> 631
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 111..434

<221> sig_peptide
<222> 111..185
<223> Von Heijne matrix
score 3.90000009536743
seq WIAAVTIAAGTAA/IG

<221> polyA_site
<222> 618..631

<400> 364
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aatcgcggag tcggtgcttt agtacgccgc tggcaccttt actctcgccg gccgcgcgaa      60
cccgtttgag ctcggtatcc tagtgcacac gccttgcaag cgacggcgcc atg agt        116
                                                       Met Ser
                                                       -25
ctg act tcc agt tcc agc gta cga gtt gaa tgg atc gca gca gtt acc       164
Leu Thr Ser Ser Ser Ser Val Arg Val Glu Trp Ile Ala Ala Val Thr
            -20                 -15                 -10
att gct gct ggg aca gct gca att ggt tat cta gct tac aaa aga ttt       212
Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys Arg Phe
        -5                  1               5
tat gtt aaa gat cat cga aat aaa gct atg ata aac ctt cac atc cag       260
Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His Ile Gln
10                  15                  20                  25
aaa gac aac ccc aag ata gta cat gct ttt gac atg gag gat ttg gga       308
Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp Leu Gly
                30                  35                  40
gat aaa gct gtg tac tgc cgt tgt tgg agg tcc aaa aag ttc cca ttc       356
Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe Pro Phe
            45                  50                  55
tgt gat ggg gct cac aca aaa cat aac gaa gag act gga gac aat gtg       404
Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp Asn Val
        60                  65                  70
ggc cct ctg atc atc aag aaa aaa gaa act taaatggaca cttttgatgc         454
Gly Pro Leu Ile Ile Lys Lys Lys Glu Thr
    75                  80
tgcaaatcag cttgtcgtga agttacctga ttgtttaatt araatgacta ccacctctgt     514
ctgattcacc ttcgctggat tctaaatgtg gtatattgcm aactgcagct ttcacattta     574
tggcatttgt cttgttgaaa catcgtggtg cacatttgtt taaacaaaaa aaaaaaa        631
```

<210> 365
<211> 781
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 19..567

<221> sig_peptide
<222> 19..63
<223> Von Heijne matrix
score 8.39999961853027
seq AMWLLCVALAVLA/WG

<221> polyA_signal

<222> 749..754

<221> polyA_site
<222> 771..781

<400> 365
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aagtgctgct tacccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg      51
                    Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu
                    -15                 -10                 -5
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga      99
Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg
                1               5                   10
atg aag agt cgg gag cag gga aga cgg ctg gga gcc gaa agc cgg acc     147
Met Lys Ser Arg Glu Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr
    15                  20                  25
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc     195
Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro
    30                  35                  40
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc     243
Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys
45                  50                  55                  60
ttc tct gca gga aat tac tac aat caa gga gag act cgt aag aaa gaa     291
Phe Ser Ala Gly Asn Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu
                65                  70                  75
ctt ttg car agc tgt gat gtt ttg ggg att cca ctc tcc agt gta atg     339
Leu Leu Gln Ser Cys Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met
            80                  85                  90
att att gac aac agg gat ttc cca rat gac cca ggc atg cag tgg gac     387
Ile Ile Asp Asn Arg Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp
    95                  100                 105
aca rag cac gtg gcc ara gtc ctc ctt cag cac ata gaa gtg aat ggc     435
Thr Xaa His Val Ala Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly
    110                 115                 120
atc aat ctg gtg gtg act ttc gat gca ggg gga rta agt ggc cac agc     483
Ile Asn Leu Val Val Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser
125                 130                 135                 140
aat cac att gct ctg tat gca gct gtg agg aag ctt gag ggc caa att     531
Asn His Ile Ala Leu Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile
                145                 150                 155
tgc aag ccc tgt ggc act gga caa gac ttt aag gaa tgagtgctgt          577
Cys Lys Pro Cys Gly Thr Gly Gln Asp Phe Lys Glu
            160                 165
caatcagtgt gcctccacct tcaccatctt cttcccctta ctctcacttc cgtcatgtgt   637
tttatacaac tctcaaatct ttcttggaga aggaggatat acatacataa tatgaaatgt   697
gtttgttctt cacagtcacc cgattttact gatatttatt tgcattttac caataaaaag   757
aaaatgcaag ctcaaaaaaa aaaa                                           781
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<210> 366
<211> 931
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 19..312

<221> sig_peptide
<222> 19..63
<223> Von Heijne matrix
score 8.39999961853027

seq AMWLLCVALAVLA/WG

<221> polyA_signal
<222> 896..901

<221> polyA_site
<222> 921..931

<400> 366

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aagtgctgct tacccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg        51
                    Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu
                    -15                 -10                 -5
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga        99
Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg
                1               5                   10
atg aag agt cgg gag cag gga rga cgg ctg gga gcc gaa agc cgg acc       147
Met Lys Ser Arg Glu Gln Gly Xaa Arg Leu Gly Ala Glu Ser Arg Thr
        15                  20                  25
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc       195
Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro
    30                  35                  40
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc       243
Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys
45                  50                  55                  60
ttc tct gca gtt ttc cgt agg gag cta agt gaa tac acc gaa rgt ctt       291
Phe Ser Ala Val Phe Arg Arg Glu Leu Ser Glu Tyr Thr Glu Xaa Leu
                65                  70                  75
acc tct gaa ccc ctc ama gcc tagggacagg arcggccggc ttacctggtg          342
Thr Ser Glu Pro Leu Xaa Ala
            80
ggttgggga cgtcggcagc tcrcgtacta cgccagcagg attganganc acagaaacag      402
ttgchsttgg ttgtattcag tacctkcatt tccgttggga actccaccwg tacttgttat    462
kctgtggaac ttttttttat ttgtagaagg agcaagaata ttgaccttac tatatagcac    522
acgaaacaat ctatgctgta tcgtgcctgc tcaatcctta aagttaactt ctaatgatag    582
taaaaracct tcctgctgcc tttaaaatgc agcttgtgct aktaacatgc atgtgtcaaa    642
ttgaaraatt agacatagat gactaratar aaagtaattt tgtaggtaat tttaragttc    702
aactccaccc agctttcakt gaaggaacct ttcaaataat aratttttgc ttaccatara    762
raaaaratca aatgacaaag caaatattga ccattaagct ggaatatggt gataattgaa    822
cagttgtata aatgaaktaa ttgaattgta cacatacaat gggtgaattt tatggcatgt    882
caaagtatac ctcaataaag ctattttttt aaattgcmaa aaaaaaaa                 931
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<210> 367
<211> 849
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 64..612

<221> sig_peptide
<222> 64..234
<223> Von Heijne matrix
score 3.79999995231628
seq QLWLVMEFCGAGS/VT

<221> polyA_site
<222> 839..849

<400> 367

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acatacgggc aagtttataa gggtcgtcat gtcaaaacgg gccagcttgc agccatcaag     60
gtt atg gat gtc aca ggg gat gaa gag gaa gaa atc aaa caa gaa att     108
    Met Asp Val Thr Gly Asp Glu Glu Glu Glu Ile Lys Gln Glu Ile
            -55                 -50                 -45
aac atg ttg aag aaa tat tct cat cac cgg aat att gct aca tac tat     156
Asn Met Leu Lys Lys Tyr Ser His His Arg Asn Ile Ala Thr Tyr Tyr
        -40                 -35                 -30
ggt gct ttt atc aaa aag aac cca cca ggc atg gat gac caa ctt tgg     204
Gly Ala Phe Ile Lys Lys Asn Pro Pro Gly Met Asp Asp Gln Leu Trp
    -25                 -20                 -15
ttg gtg atg gag ttt tgt ggt gct ggc tct gtc acc gac ctg atc aag     252
Leu Val Met Glu Phe Cys Gly Ala Gly Ser Val Thr Asp Leu Ile Lys
-10                  -5                   1               5
aac aca aaa ggt aac acg ttg aaa gag gag tgg att gca tac atc tgc     300
Asn Thr Lys Gly Asn Thr Leu Lys Glu Glu Trp Ile Ala Tyr Ile Cys
            10                  15                  20
msg gaa atc tta cgg ggg ctg art cac ctg cac cag cat aaa gtg att     348
Xaa Glu Ile Leu Arg Gly Leu Xaa His Leu His Gln His Lys Val Ile
        25                  30                  35
cat cga rat att aaa ggg caa aat gtc ttg ctg act gaa aat gca gaa     396
His Arg Xaa Ile Lys Gly Gln Asn Val Leu Leu Thr Glu Asn Ala Glu
    40                  45                  50
gtt aaa cta gtg gac ttt gga rtc akt gct cag ctt gat cga aca gtg     444
Val Lys Leu Val Asp Phe Gly Xaa Xaa Ala Gln Leu Asp Arg Thr Val
55                  60                  65                  70
ggc agg arg aat act ttc att gga act ccc tac tgg atg gca cca raa     492
Gly Arg Xaa Asn Thr Phe Ile Gly Thr Pro Tyr Trp Met Ala Pro Xaa
                75                  80                  85
gtt att gcc tgt gat gaa aac cca sat gcc aca tat gat ttc aar art     540
Val Ile Ala Cys Asp Glu Asn Pro Xaa Ala Thr Tyr Asp Phe Lys Xaa
            90                  95                  100
gac ttg tgg tct ttg ggt atc acc gcc att gaa atg gca gaa ggg ctc     588
Asp Leu Trp Ser Leu Gly Ile Thr Ala Ile Glu Met Ala Glu Gly Leu
        105                 110                 115
ccc ctc tct gtg aca tgc acc cca tgagagctct cttcctcatc ccccggaatc    642
Pro Leu Ser Val Thr Cys Thr Pro
    120                 125
cagcgcctcg gctgaagtct aagaagtggt caaaaaaatt ccagtcattt attgagagct   702
gcttggtaaa aaatcacagc cagcgaccag caacagaaca attgatgaag catccattta   762
tacgagacca acctaatgag cgacaggtcc gcattcaact caaggaccat attgatagaa   822
caaagaagaa gcgaggaaaa aaaaaaa                                        849
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<210> 368
<211> 644
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 39..458

<221> sig_peptide
<222> 39..80
<223> Von Heijne matrix
score 4.40000009536743
seq FLTALLWRGRIPG/RQ

<221> polyA_signal
<222> 613..618

<221> polyA_site
<222> 633..644

<400> 368
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agcggagacg cagagtcttg agcagcgcgn caggcacc atg ttc ctg act gcg ctc      56
                                          Met Phe Leu Thr Ala Leu
                                                          -10
ctc tgg cgc ggc cgc att ccc ggc cgt cag tgg atc ggg aag cac cgg     104
Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln Trp Ile Gly Lys His Arg
            -5                  1               5
cgg ccg cgg ttc gtg tcg ttg cgc gcc aag cag aac atg atc cgc cgc     152
Arg Pro Arg Phe Val Ser Leu Arg Ala Lys Gln Asn Met Ile Arg Arg
    10                  15                  20
ctg gag atc gag gcg gag aac cat tac tgg ctg agc atg ccc tac atg     200
Leu Glu Ile Glu Ala Glu Asn His Tyr Trp Leu Ser Met Pro Tyr Met
25                  30                  35                  40
acc cgg gag cag gag cgc ggc cac gcc gcg ttg cgc agg agg gag gcc     248
Thr Arg Glu Gln Glu Arg Gly His Ala Ala Leu Arg Arg Arg Glu Ala
                45                  50                  55
ttc gag gcc ata aag gcg gcc gcc act tcc aag ttc ccc ccg cat aga     296
Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser Lys Phe Pro Pro His Arg
            60                  65                  70
ttc att gcg gac cag ctc gac cat ctc aat vgt cac caa gaa atg gtc     344
Phe Ile Ala Asp Gln Leu Asp His Leu Asn Xaa His Gln Glu Met Val
        75                  80                  85
cta atc ctg agt cgt cac cct tgg att tta tgg atc acg gag ctg acc     392
Leu Ile Leu Ser Arg His Pro Trp Ile Leu Trp Ile Thr Glu Leu Thr
    90                  95                  100
atc ttt acc tgg tct gga ctg aaa aac tgt agc ttg tgt gaa aat gag     440
Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys Ser Leu Cys Glu Asn Glu
105                 110                 115                 120
ctt tgg acc agt ctt tat taaaacaaac aaacatgagt agtctgcata            488
Leu Trp Thr Ser Leu Tyr
                125
tcgaatatct agagctctaa acccccaat acttaaaagt ctaattgctg tcctgtggtt    548
tcattagtct gataggaaga tagggatttc ctcagtcaca gatgatattt tgaaggaaag   608
ctgcaataaa gccacaatga tttgaaaaaa aaaaaa                             644
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<210> 369
<211> 918
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 9..185

<221> sig_peptide
<222> 9..50
<223> Von Heijne matrix
score 3.70000004768372
seq AALVTVLFTGVRR/LH

<221> polyA_site
<222> 906..918

<400> 369
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agctcagc atg gct gct tta gtg act gtt ctc ttc aca ggt gtc cgg agg      50
         Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg
                         -10                 -5
```

ctg cac tgc agc gcr scg ctt ggg cgg gcg gcc agt ggc grc tac agc 98
Leu His Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser
1 5 10 15
agg aac tgg ctg cca acc cct ccg gct acg ggc ccc tta ccg agc tcc 146
Arg Asn Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser
20 25 30
cag act ggt cat atg cgg atg gcc gcc ctg ctc ccc caa tgaaaggcca 195
Gln Thr Gly His Met Arg Met Ala Ala Leu Leu Pro Gln
35 40 45
gcttcgaaaa aaagctgaaa gggagacktt tgcaaracra kttgtactgc tgtcacagga 255
aatggacgct ggattacaas catggcasct caggcagcar aakttgcagg aaraacaaag 315
gaagcaggaa aatgctctta aacccaaagg ggcttcactg aaaascccac ttccaaktca 375
ataaaaagca actcctgcct cccttcctca ccctgtctct ggatttcttt tctatcacct 435
aratgcttca tccagccara aaatagcctt cackktcccc atctgtcttc aragcaaaar 495
agctgggacm ccaaraacaa gctgttarat cactgcctgg gaggcttggc ttartactct 555
catctctggt tccattccag ttcagctaag tcttgcttta aaatttttac ctcctagctg 615
ggtgcggtgg ctcacgcctg taatcccagc actttgggag gctgaggcgg gcagatcaca 675
agatcaggag ttcgagacca gcctggccaa cccagcctgg tcaacatggt gaaaccctgt 735
ccctactaaa gatacaaaca attagccggg cgtggtgggg tgcgcttgta atcccagcta 795
ctcaggaggc tgaggcagga gaatcgctta aactcgggag gtagaggttg cagtgagcca 855
aggtcacacc attgcactcc aacctgggcg acagggcgag actctgtctc aaaaaaaaaa 915
aaa 918

<210> 370
<211> 472
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 14..316

<221> sig_peptide
<222> 14..121
<223> Von Heijne matrix
score 5.19999980926514
seq PLRLLNLLILIEG/SV

<221> polyA_signal
<222> 442..447

<221> polyA_site
<222> 458..471

<400> 370
attatataga gcc atg ggg cct tac aac gtg gca gtg cct tca gat gta 49
Met Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val
-35 -30 -25
tct cat gcc cgc ttt tat ttc tta ttt cat cga cca tta agg ctg tta 97
Ser His Ala Arg Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu
-20 -15 -10
aat ctg ctc atc ctt att gag ggc agt gtc gtc ttc tat cag ctc tat 145
Asn Leu Leu Ile Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr
-5 1 5
tcc ttg ctg cgg tcg gag aag tgg aac cac aca ctt tcc atg gct ctc 193
Ser Leu Leu Arg Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu
10 15 20
atc ctc ttc tgc aac tac tat gtt tta ttt aaa ctt ctc cgg gac aga 241
Ile Leu Phe Cys Asn Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg
25 30 35 40

```
wta kta tta ggc agg gca tac tcc tac cca ctc aac agt tat gaa ctc      289
Xaa Xaa Leu Gly Arg Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu
                45                  50                  55
aag gca aac twa gct gcc tct caw caa tgagggagaa ctcagataaa            336
Lys Ala Asn Xaa Ala Ala Ser Xaa Gln
            60                  65
aatattttca tacgttctat tttttcttg tgatttttat aaatatttaa gatattttat     396
attttgtata ctattatgtt ttgaaagtcg ggaagagtaa gggatattaa atgtatccgt    456
aaacaaaaaa aaaaam                                                    472
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<210> 371
<211> 1504
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 70..1092

<221> sig_peptide
<222> 70..234
<223> Von Heijne matrix
score 4.09999990463257
seq AVCAALLASHPTA/EV

<221> polyA_signal
<222> 1475..1480

<221> polyA_site
<222> 1493..1504

<400> 371

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agaaatcgta ggacttccga aagcagcggc ggcgtttgct tcactgcttg gaagtgtgag     60
tgcgcgaag atg cga aag gtg gtt ttr att acc ggg gct agc agt ggc att    111
          Met Arg Lys Val Val Leu Ile Thr Gly Ala Ser Ser Gly Ile
          -55                 -50                 -45
ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat      159
Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His
    -40                 -35                 -30
ctg tgt ttg gcg tgc agg aat atg agc aag gca gaa gct gtc tgt gct      207
Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala
-25                 -20                 -15                 -10
gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg      255
Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val
                -5                  1               5
gat gtc agc aac ctg cag tca ttc ttc cgg gcc tcc aag gaa ctt aag      303
Asp Val Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys
        10                  15                  20
caa agg ttt cag aga tta gac tgt ata tat cta aat gct ggg atc atg      351
Gln Arg Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met
    25                  30                  35
cct aat cca caa cta aat atc aaa gca ctt ttc ttt ggc ctc ttt tca      399
Pro Asn Pro Gln Leu Asn Ile Lys Ala Leu Phe Phe Gly Leu Phe Ser
40                  45                  50                  55
aga aaa gtg att cat atg ttc tcc aca gct gaa ggc ctg ctg acc cag      447
Arg Lys Val Ile His Met Phe Ser Thr Ala Glu Gly Leu Leu Thr Gln
                60                  65                  70
ggt gat aag atc act gct gat gga ctt cag gag gtg ttt gag acc aat      495
Gly Asp Lys Ile Thr Ala Asp Gly Leu Gln Glu Val Phe Glu Thr Asn
            75                  80                  85
```

```
gtc ttt ggc cat ttt atc ctg att cgg gaa ctg gag cct ctc ctc tgt        543
Val Phe Gly His Phe Ile Leu Ile Arg Glu Leu Glu Pro Leu Leu Cys
         90                  95                 100
cac agt gac aat cca tct cag ctc atc tgg aca tca tct cgc agt gca        591
His Ser Asp Asn Pro Ser Gln Leu Ile Trp Thr Ser Ser Arg Ser Ala
    105                 110                 115
agg aaa tct aat ttc agc ctc gag gac ttc cag cac agc aaa ggc aag        639
Arg Lys Ser Asn Phe Ser Leu Glu Asp Phe Gln His Ser Lys Gly Lys
120                 125                 130                 135
gaa ccc tac agc tct tcc aaa tat gcc act gac ctt ttg agt gtg gct        687
Glu Pro Tyr Ser Ser Ser Lys Tyr Ala Thr Asp Leu Leu Ser Val Ala
                140                 145                 150
ttg aac agg aac ttc aac cag cag ggt ctc tat tcc aat gtg gcc tgt        735
Leu Asn Arg Asn Phe Asn Gln Gln Gly Leu Tyr Ser Asn Val Ala Cys
            155                 160                 165
cca ggt aca gca ttg acc aat ttg aca tat gga att ctg cct ccg ttt        783
Pro Gly Thr Ala Leu Thr Asn Leu Thr Tyr Gly Ile Leu Pro Pro Phe
        170                 175                 180
ata tgg acg ctg ttg atg ccg gca ata ttg cta ctt cgc ttt ttt gca        831
Ile Trp Thr Leu Leu Met Pro Ala Ile Leu Leu Leu Arg Phe Phe Ala
    185                 190                 195
aat gca ttc act ttg aca cca tat aat gga aca gaa gct ctg gta tgg        879
Asn Ala Phe Thr Leu Thr Pro Tyr Asn Gly Thr Glu Ala Leu Val Trp
200                 205                 210                 215
ctt ttc cac caa aag cct gaa tct ctc aat cct ctg atc aaa tat ctg        927
Leu Phe His Gln Lys Pro Glu Ser Leu Asn Pro Leu Ile Lys Tyr Leu
                220                 225                 230
agt gcc acc act ggc ttt gga aga aat tac att atg acc cag aag atg        975
Ser Ala Thr Thr Gly Phe Gly Arg Asn Tyr Ile Met Thr Gln Lys Met
            235                 240                 245
gac cta gat gaa gac act gct gaa aaa ttt tat caa aag tta ctg gaa       1023
Asp Leu Asp Glu Asp Thr Ala Glu Lys Phe Tyr Gln Lys Leu Leu Glu
        250                 255                 260
ctg gaa aag cac att agg gtc act att caa aaa aca gat aat cag gcc       1071
Leu Glu Lys His Ile Arg Val Thr Ile Gln Lys Thr Asp Asn Gln Ala
    265                 270                 275
agg ctc agt ggc tca tgc cta taattccagc actttgggag gccaaggcag          1122
Arg Leu Ser Gly Ser Cys Leu
280                 285
aaggatcact tgagaccagg agttcaagac cagcctgaga aacatagtga gcccttgtct     1182
ctacaaaaag aaataaaaat aatagctggg tgtggtggca tgcgcatgta gtcccagcta     1242
ctcagaagga tgaggtggga ggatctcttg aggctgggag gcagaggttg cagtgagctg     1302
agattgtgcc actgcactcc agcctgggtg acagcgagac cctgtctcaa aatatgtata     1362
tatttaatat atatataaaa ccagagctga caatgacact ctggaacatt gcataccttc     1422
tgtacattct ggggtacatg gatttctact gagttggata atatgcattt gtaataaact     1482
atgaactatg aaaaaaaaaa aa                                              1504
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<210> 372
<211> 765
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 274..597

<221> sig_peptide
<222> 274..399
<223> Von Heijne matrix
score 5.19999980926514

seq LLFDLVCHEFCQS/DD

<221> polyA_signal
<222> 731..736

<221> polyA_site
<222> 754..765

<400> 372
accaggaaca tccagctatt tatgatagca tttgcttcat tatgtcaagt tcaacaaatg 60
ttgacttgct ggtgaaggtg ggggaggttg tggacaagct ctttgatttg gatgagaaac 120
taatgttaag aatgggtcag aaatggggct gctcagcctc tggaccaacc ccaggaagag 180
tctgaagagc agccagtgtt tcggcttgtg ccctgtatac ttgaagctgc caaacaagta 240
cgttctgaaa atccagaatg gcttgatgtt tac atg cac att tta caa ctg ctt 294
Met His Ile Leu Gln Leu Leu
-40
act aca gtg gat gat gga att caa gca att gta cat tgt cct gac act 342
Thr Thr Val Asp Asp Gly Ile Gln Ala Ile Val His Cys Pro Asp Thr
-35 -30 -25 -20
gga aaa gac att tgg aat tta ctt ttt gac ctg gtc tgc cat gaa ttc 390
Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp Leu Val Cys His Glu Phe
-15 -10 -5
tgc cag tct gat gat cca gcc atc att ctt caa raa car aaa acr gtg 438
Cys Gln Ser Asp Asp Pro Ala Ile Ile Leu Gln Xaa Gln Lys Thr Val
1 5 10
cta gcc tct gtt ttt tca gtg ttg tct gcc atc tat gcc tca cag act 486
Leu Ala Ser Val Phe Ser Val Leu Ser Ala Ile Tyr Ala Ser Gln Thr
15 20 25
gag caa gak tat cta aar ata raa aaa gga gac ggt ggc tca ggg agt 534
Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys Gly Asp Gly Gly Ser Gly Ser
30 35 40 45
aaa gga agg cca ktt gan caa aca gaa ktg ttc ctc tgc att tca aaa 582
Lys Gly Arg Pro Xaa Xaa Gln Thr Glu Xaa Phe Leu Cys Ile Ser Lys
50 55 60
cct tct tcc ttt cta tagccctgtg gtggaagatt ttattaaaat cctacgtgaa 637
Pro Ser Ser Phe Leu
65
gttgataagg cgcttgctga tgacttggaa aaaaacttcc caagtttgaa ggttcagact 697
taaaacctga attggaatta cttctgtaca agaaataaac tttatttttc tcactgacaa 757
aaaaaaaa 765

<210> 373
<211> 1041
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 230..469

<221> sig_peptide
<222> 230..307
<223> Von Heijne matrix
score 4.90000009536743
seq VLCTNQVLITARA/VP

<221> polyA_signal
<222> 1004..1009

<221> polyA_site

<222> 1027..1040

<400> 373

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aacttccaag ttgtagtgtt gttgttttca gcctgctgct gctgctgcta ttgcggctag      60
gggaaccgtc gtggggaagg atggtgtgcg aaaaatgtga aaagaaactt ggtactgtta     120
tcactccaga tacatggaaa gatggtgcta ggaataccac agaaagtggt ggaagaaagc     180
tgaatgaaaa taaagctttg acttcaaaaa aagccagaat tgatccata atg gaa gaa     238
                                                      Met Glu Glu
                                                          -25
ata agt tct cca ctt gta gaa ttt gta aaa gtt ttg tgc acc aac cag       286
Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys Thr Asn Gln
            -20                 -15                 -10
gtt ctc att act gcc agg gct gtg cct aca aaa aag gca tct gtg cga       334
Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala Ser Val Arg
        -5                  1               5
tgt gtg gaa aaa agg ttt tgg ata cca aaa act aca agc aaa cat ctg       382
Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser Lys His Leu
10                  15                  20                  25
tct aga tgt att gat gga att tct ggc ttt cta aat gat ttt act ttc       430
Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp Phe Thr Phe
                30                  35                  40
tgc ctt gaa ttt tca agg cat aga tgt caa ctt aca gaa taacatgtkt        479
Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu
            45                  50
taagataatt aagtktaaac cagaraattt gattgttact cattttgctc tcatgtkcta     539
aaacagcaac agtgtaacta gtcttttgtt gtaaatggtt atttccctta taaaaatttt     599
aaaaactaag tggcaaattc catgaaaata tttctcagtt ctgtatgcac ttttatttaa     659
cattattcat ataattctcc ccccaccact ttatttataa atactgcaaa aktgaraagg     719
agataataaa tactttgctc tgaatttggc atccaaagtt aacatttctc ccctcactcc     779
cttgctggtg tcatagttat tagaatcagc agcctcttaa ctaattgcgg tttcatagga     839
tatataaatg tttcaagcca ttattgctga atggttcttt agttattaac ctagacccaa     899
atcaaagacc agttggattt atgatatttt ttatttgttc ttgcagccaa agtgccagtt     959
tctttaatat gtgaccaaga acacaaggag catccatatg gccaaataaa tacactgaat    1019
tttagaaaaa caaaaaaaaa ar                                             1041
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<210> 374
<211> 1164
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 72..545

<221> sig_peptide
<222> 72..203
<223> Von Heijne matrix
score 5.5
seq ILFFTGWWIMIDA/AV

<221> polyA_site
<222> 1151..1162

<400> 374

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aaagtcggcg tggacgtttg aggaagctgg gatacagcat ttaatgaaaa atttatgctt      60
aagaagtaaa a atg gca ggc ttc cta gat aat ttt cgt tgg cca gaa tgt      110
             Met Ala Gly Phe Leu Asp Asn Phe Arg Trp Pro Glu Cys
                         -40                 -35
gaa tgt att gac tgg agt gag aga aga aat gct gtg gca tct gtt gtc       158
Glu Cys Ile Asp Trp Ser Glu Arg Arg Asn Ala Val Ala Ser Val Val
```

```
 -30                 -25                 -20
gca ggt ata ttg ttt ttt aca ggc tgg tgg ata atg att gat gca gct      206
Ala Gly Ile Leu Phe Phe Thr Gly Trp Trp Ile Met Ile Asp Ala Ala
-15                 -10                  -5                   1
gtg gtg tat cct aag cca gaa cag ttg aac cat gcc ttt cac aca tgt      254
Val Val Tyr Pro Lys Pro Glu Gln Leu Asn His Ala Phe His Thr Cys
              5                  10                  15
ggt gta ttt tcc aca ttg gct ttc ttc atg ata aat gct gta tcc aat      302
Gly Val Phe Ser Thr Leu Ala Phe Phe Met Ile Asn Ala Val Ser Asn
         20                  25                  30
gct cag gtg aga ggt gat agc tat gaa agc ggc tgt tta gga aga aca      350
Ala Gln Val Arg Gly Asp Ser Tyr Glu Ser Gly Cys Leu Gly Arg Thr
     35                  40                  45
ggt gct cga gtt tgg ctt ttc att ggt ttc atg ttg atg ttt ggg tca      398
Gly Ala Arg Val Trp Leu Phe Ile Gly Phe Met Leu Met Phe Gly Ser
50                  55                  60                  65
ctt att gct tcc atg tgg att ctt ttt ggt gca tat gtt acc caa aat      446
Leu Ile Ala Ser Met Trp Ile Leu Phe Gly Ala Tyr Val Thr Gln Asn
                 70                  75                  80
act gat gtt tat ccg gga cta gct gtg ttt ttt caa aat gca ctt ata      494
Thr Asp Val Tyr Pro Gly Leu Ala Val Phe Phe Gln Asn Ala Leu Ile
             85                  90                  95
ttt ttt agc act ctg atc tac aaa ttt gga aga acc gaa gag cta tgg      542
Phe Phe Ser Thr Leu Ile Tyr Lys Phe Gly Arg Thr Glu Glu Leu Trp
        100                 105                 110
acc tgagatcact tcttaagtca cattttcctt ttgttatatt ctgtttgtag           595
Thr
ataggttttt tatctctcag tacacattgc caaatggagt agattgtaca ttaaatgttt    655
tgtttcttta catttttatg ttctgagttt tgaaatagtt ttatgaaatt tctttatttt    715
tcattgcata gactgttaat atgtatataa tacaagacta tatgaattgg ataatgagta    775
tcagtttttt attcctgaga tttagaactt gatctactcc ctgagccagg gttacatcat    835
cttgtcattt tagaagtaac cactcttgtc tctctggctg ggcacggtgg ctcatgcctg    895
taatcccagc actttgggag gccgaggcgg gccgattgct tgaggtcaag tgtttgagac    955
cagcctggcc aacatggcga accccatct actaaaaata caaaaattag ccaggcatgg    1015
tggtgggtgc ctgtaatccc aactacctag gaggctgagg caggagaatc gcttgaaccc   1075
gggggcaga ggttgyagtg agctgagttt gcgccactgc actctagcct gggggagaaa    1135
gtgaaactcc ctctcaaaaa aaaaaaamc                                     1164
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<210> 375
<211> 1250
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 36..425

<221> sig_peptide
<222> 36..119
<223> Von Heijne matrix
score 11.6000003814697
seq LLLLVQLLRFLRA/DG

<221> polyA_signal
<222> 1215..1220

<221> polyA_site
<222> 1240..1250

<400> 375

atttcttccc cccgagctgg gcgtgcgcgg ccgca atg aac tgg gag ctg ctg 53
Met Asn Trp Glu Leu Leu
-25
ctg tgg ctg ctg gtg ctg tgc gcg ctg ctc ctg ctc ttg gtg cag ctg 101
Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu Leu Val Gln Leu
-20 -15 -10
ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta cta tgg gcc gag 149
Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu Leu Trp Ala Glu
-5 1 5 10
tgg cag gga cga cgc cca gaa tgg gag ctg act gat atg gtg gtg tgg 197
Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp Met Val Val Trp
15 20 25
gtg act gga gcc tcg agt gga att ggt gag gag ctg gct tac cag ttg 245
Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu Ala Tyr Gln Leu
30 35 40
tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga aga gtg cat gag 293
Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg Arg Val His Glu
45 50 55
ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc aat tta aaa gaa 341
Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly Asn Leu Lys Glu
60 65 70
aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac act ggt tcc cat 389
Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp Thr Gly Ser His
75 80 85 90
gaa agc ggc tac caa agc tgt tct cca gga att tgg tagaatcgac 435
Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly Ile Trp
95 100
attctggtca acaatgtgga aatgtcccag cgttctctgt gcatggatac caacttggat 495
gtctacagaa agctaatgag agcttaacta cttagggacg gtgtccttga caaaatgtgk 555
kctgcctcac atgatcgaga ngaarcaagg aaagattgtt actgtgaata gcatcctggg 615
tatcatatct gtacctcttt ccattggata ctgtgctagc aagcatgctc tccggggktk 675
ktttaatggc cttcraacag aacttgccac atacccargt ataatagttt ctaacatttg 735
cccaggacct gtgcaatcaa atattgtgga aaattcccta gctggagaag tcacaaagac 795
tataggcaat aatggagacc agtcccacaa gatgacaacc agtcgttgtg tgcggctgat 855
gttaatcagc atggccaatg atttgaaaga agtttggatc tcagaacaac ctttcttgtt 915
agtaacatat ttgtggcaat acatgccaac ctgggcctgg tggataacca acaagatggg 975
gaagaaaagg attgagaact ttaagagtgg tgtggatgca gactcttctt attttaaaat 1035
ctttaagaca aaacatgact gaaaagagca cctgtacttt tcaagccact ggagggagaa 1095
atggaaaaca tgaaaacagc aatcttctta tgcttctgaa taatcaaaga ctaatttgtg 1155
attttacttt ttaatagata tgactttgct tccaacatgg aatgaaataa aaaataaata 1215
ataaaagatt gccatgaatc ttgcaaaaaa aaaaa 1250

<210> 376
<211> 947
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 155..751

<221> sig_peptide
<222> 155..340
<223> Von Heijne matrix
score 3.70000004768372
seq SILGIISVPLSIG/YC

<221> polyA_signal
<222> 912..917

<221> polyA_site
<222> 937..947

<400> 376
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agtgaaaaga agatgcctag agaatggcaa tttaaaagaa aaagatatac ttgttttgcc      60
ccttgacctg accgacactg gttcccatga agcggctacc aaagctgttc tccaggagtt     120
tggtagaatc gacattctgg tcaacaatgg tgga atg tcc cag cgt tct ctg tgc     175
                                      Met Ser Gln Arg Ser Leu Cys
                                                  -60
atg gat acc agc ttg gat gtc tac aga rag cta ata gag ctt aac tac       223
Met Asp Thr Ser Leu Asp Val Tyr Arg Xaa Leu Ile Glu Leu Asn Tyr
-55                 -50                 -45                 -40
tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc gag       271
Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile Glu
                -35                 -30                 -25
agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc ata       319
Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile Ile
            -20                 -15                 -10
tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc cgg       367
Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu Arg
        -5                  1               5
ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt ata       415
Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly Ile
10                  15                  20                  25
ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg gaa       463
Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val Glu
                30                  35                  40
aat tcc cta gct gga gaa gtc aca aaa act ata ggc aat aat gga aac       511
Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly Asn
            45                  50                  55
cag tcc cac aag atg aca acc agt cgt tgt gtg cgg ctg atg tta atc       559
Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu Ile
        60                  65                  70
agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct ttc       607
Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro Phe
    75                  80                  85
ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg tgg       655
Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp Trp
90                  95                  100                 105
ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt ggt       703
Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser Gly
                110                 115                 120
gtg gat gcm rac tct tct tat ttt aaa atc ttt aag aca aaa cat gac       751
Val Asp Ala Xaa Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His Asp
            125                 130                 135
tgaaaaganc acctgtactt ttcaagccac tggagggaga aatggaaaac atgaaaacag     811
caatcttctt atgcttctga ataatcaaag actaatttgt gattttactt tttaatagat     871
atgactttgc ttccaacatg grrtgaaata aaaaataaat aataaaagat tgccatgrrt     931
cttgcaaaaa aaaaaa                                                     947
```

<210> 377
<211> 621
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..585

<221> sig_peptide

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<222> 46..120
<223> Von Heijne matrix
      score 6.30000019073486
      seq AFSLSVMAALTFG/CF

<221> polyA_signal
<222> 584..589

<221> polyA_site
<222> 606..619

<400> 377
aactgggtgt gcgtrtggag tccggactcg tgggagacga tcgcg atg aac acg gtg      57
                                                  Met Asn Thr Val
                                                  -25
ctg tcg cgg gcg aac tca ctg ttc gcc ttc tcg ctg agc gtg atg gcs       105
Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu Ser Val Met Ala
    -20                 -15                 -10
gcg ctc acc ttc ggc tgc ttc atc ayy acc gcc ttc aaa gac agg agc       153
Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe Lys Asp Arg Ser
-5                  1               5                   10
gtc ccg gtg cgg ctg cac gtc tcg cga atc atg cta aaa aat gta gaa       201
Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu Lys Asn Val Glu
            15                  20                  25
gat ttc act gga cct aga gaa aga agt gat ctg gga ttt atc aca ttt       249
Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly Phe Ile Thr Phe
        30                  35                  40
gat ata act gct gat cta gag aat ata ttt gat tgg aat gtt aag cag       297
Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp Asn Val Lys Gln
    45                  50                  55
ttg ttt ctt tat tta tca gca gaa tat tca aca aaa aat aat gct ctg       345
Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys Asn Asn Ala Leu
60                  65                  70                  75
aac caa ktt gtc cta tgg gac aag att gtt ttg aga ggt gat aat ccg       393
Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg Gly Asp Asn Pro
                80                  85                  90
aag ctg ctg ctg aaa gat atg aaa aca aaa tat ttt ttc ttt gac gat       441
Lys Leu Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe Phe Phe Asp Asp
            95                  100                 105
gga aat ggt ctc wag gga aac agg aat gtc act ttg acc ctg tct tgg       489
Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu Thr Leu Ser Trp
        110                 115                 120
aac gtc gta cca aat gct gga att cta cct ctt gtg aca gga tca gga       537
Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val Thr Gly Ser Gly
    125                 130                 135
cac gta tct gtc cca ttt cca gat aca tat gaa ata acg aag agt tat       585
His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile Thr Lys Ser Tyr
140                 145                 150                 155
taaattattc tgaatttgaa acaaaaaaaa aaaahm                               621


<210> 378
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 378
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Met Pro Ser Val Asn Ser Ala Gly Leu Cys Val Leu Gln Leu Thr Thr
-20 -15 -10 -5
Ala Val Thr Ser Ala Phe Leu Leu Ala Lys Val Asn Pro Phe Glu Xaa
1 5 10
Phe Leu Ser Arg Gly Phe Trp Leu Cys Ala Ala His His Phe Ile His
15 20 25
Pro Cys Leu Asp
30

<210> 379
<211> 193
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -23..-1

<400> 379
Met Val Val Leu Arg Ala Gly Lys Lys Thr Phe Leu Pro Pro Leu Xaa
-20 -15 -10
Arg Ala Phe Ala Cys Arg Gly Cys Gln Leu Ala Pro Glu Arg Gly Ala
-5 1 5
Glu Arg Arg Asp Thr Ala Pro Ser Gly Val Ser Arg Phe Cys Pro Pro
10 15 20 25
Arg Lys Ser Cys His Asp Trp Ile Gly Pro Pro Asp Lys Tyr Ser Asn
30 35 40
Leu Arg Pro Val His Phe Tyr Ile Pro Glu Asn Glu Ser Pro Leu Glu
45 50 55
Gln Lys Leu Arg Lys Leu Arg Gln Glu Thr Gln Glu Trp Asn Gln Gln
60 65 70
Phe Trp Ala Asn Gln Asn Leu Thr Phe Ser Lys Glu Lys Glu Glu Phe
75 80 85
Ile His Ser Arg Leu Lys Thr Lys Gly Leu Gly Leu Arg Thr Glu Ser
90 95 100 105
Gly Gln Lys Ala Thr Leu Asn Ala Glu Glu Met Ala Asp Phe Tyr Lys
110 115 120
Glu Phe Leu Ser Lys Asn Phe Gln Lys His Met Tyr Tyr Asn Arg Asp
125 130 135
Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly Lys Val Ala
140 145 150
Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys Lys Arg Ser
155 160 165
Asn
170

<210> 380
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -14..-1

<400> 380
Met Ala Phe Thr Leu Xaa Ser Leu Leu Gln Ala Ala Leu Leu Cys Val
-10 -5 1

Asn Ala Ile Ala Val Leu His Glu Glu Arg Phe Leu Lys Asn Ile Gly
5 10 15
Trp Gly Thr Asp Gln Gly Ile Gly Gly Phe Gly Glu Glu Pro Gly Ile
20 25 30
Lys Ser Xaa Xaa Met Xaa Leu Ile Arg Ser Val Arg Thr Val Met Arg
35 40 45 50
Val Pro Leu Ile Ile Val Asn Ser Ile Ala Ile Val Leu Leu Leu Leu
55 60 65
Phe Gly

<210> 381
<211> 198
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 381
Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr
-20 -15 -10
Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His
-5 1 5 10
Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala
15 20 25
Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Arg Leu Thr Lys Ala Arg
30 35 40
Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu
45 50 55
Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu
60 65 70 75
Glu Thr Gln Met Glu Glu Asp Ile Leu Xaa Leu Gln Ala Xaa Ala Thr
80 85 90
Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp
95 100 105
Ser Val Gln Arg Leu Xaa Xaa Gln Leu Xaa Xaa Ala Trp Leu Gly Pro
110 115 120
Ala Tyr Arg Lys Phe Glu Val Leu Lys Ala Pro Pro Xaa Lys Gln Asn
125 130 135
His Ile Leu Trp Ala Leu Thr Gly His Val Xaa Arg Gln Xaa Arg Glu
140 145 150 155
Met Val Ala Gln Gln Xaa Xaa Leu Xaa Gln Ile Gln Glu Lys Leu His
160 165 170
Thr Ala Ala Leu Pro Ala
175

<210> 382
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -55..-1

<400> 382
Met Asp Lys Leu Lys Lys Val Leu Ser Gly Gln Asp Thr Glu Asp Arg

```
-55                 -50                 -45                 -40
Ser Gly Leu Ser Glu Val Val Glu Ala Ser Ser Leu Ser Trp Ser Thr
                -35                 -30                 -25
Arg Ile Lys Gly Phe Ile Ala Cys Phe Ala Ile Gly Ile Leu Cys Ser
            -20                 -15                 -10
Leu Leu Gly Thr Val Leu Leu Trp Val Pro Arg Lys Gly Leu His Leu
        -5                  1               5
Phe Ala Val Phe Tyr Thr Phe Gly Asn Ile Ala Ser Ile Gly Ser Thr
10                  15                  20                  25
Ile Phe Leu Met Gly Pro Val Lys Gln Leu Lys Arg Met Phe Glu Pro
                30                  35                  40
Thr Arg Leu Ile Ala Thr Ile Met Val Leu Leu Cys Phe Ala Leu Thr
            45                  50                  55
Leu Cys Ser Ala Phe Trp Trp His Asn Lys Gly Leu Ala Leu Ile Phe
        60                  65                  70
Cys Ile Leu Gln Ser Leu Ala Leu Thr Trp Tyr Ser Leu Ser Phe Ile
    75                  80                  85
Pro Phe Ala Arg Asp Ala Val Lys Xaa Cys Phe Ala Val Cys Leu Ala
90                  95                  100                 105
```

<210> 383
<211> 108
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

<400> 383

```
Met Lys Ala Leu Cys Leu Leu Leu Leu Pro Val Leu Gly Leu Leu Val
            -15                 -10                 -5
Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile Asn Glu Arg Ile
        1               5                   10
Gln Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile Ser Ser Ile Gly
15                  20                  25                  30
Arg Gly Ser Glu Ser Val Thr Ser Arg Gly Asp Leu Ala Thr Cys Pro
                35                  40                  45
Arg Gly Phe Ala Val Thr Gly Cys Thr Cys Gly Ser Ala Cys Gly Ser
            50                  55                  60
Trp Asp Val Arg Ala Glu Thr Thr Cys His Cys Gln Cys Ala Gly Met
        65                  70                  75
Asp Trp Thr Gly Ala Arg Cys Cys Arg Val Gln Pro
    80                  85                  90
```

<210> 384
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -22..-1

<400> 384

```
Met Ile Ser Arg Gln Leu Arg Ser Leu Ser Cys Leu Cys Pro Ala Leu
        -20                 -15                 -10
Phe Pro Gly Thr Ser Ser Phe Ile Val Ala Leu Ser Ser Pro Ala Asp
```

```
     -5                   1                   5                  10
Leu Tyr Ile Pro Xaa Arg Xaa Arg Ser Asp Glu Leu Val Phe Glu Ser
                15                  20                  25
Gln Lys Gly Ser Ala Met Glu Leu Ala Val Ile Thr Val Xaa Gly Val
            30                  35                  40
```

<210> 385
<211> 27
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 385

```
Met Gly Phe Leu Xaa Leu Met Thr Leu Thr Thr His Val His Ser Ser
-15                 -10                 -5                   1
Ala Lys Pro Asn Glu Gln Pro Trp Leu Leu Asn
            5                   10
```

<210> 386
<211> 186
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 386

```
Met Ser Pro Ser Gly Arg Leu Cys Leu Leu Thr Ile Val Gly Leu Ile
    -20                 -15                 -10
Leu Pro Thr Arg Gly Gln Thr Leu Lys Asp Thr Thr Ser Ser Ser Ser
-5                  1               5                   10
Ala Asp Ser Thr Ile Met Asp Ile Gln Val Pro Thr Arg Ala Pro Asp
            15                  20                  25
Ala Val Tyr Thr Glu Leu Gln Pro Thr Ser Pro Thr Pro Thr Trp Pro
        30                  35                  40
Ala Asp Glu Thr Pro Gln Pro Gln Thr Gln Thr Gln Gln Leu Glu Gly
    45                  50                  55
Thr Asp Gly Pro Leu Val Thr Asp Pro Glu Thr His Xaa Ser Xaa Lys
60                  65                  70                  75
Ala Ala His Pro Thr Asp Asp Thr Thr Thr Leu Ser Glu Arg Pro Ser
                80                  85                  90
Pro Ser Thr Xaa Val His Xaa Arg Pro Xaa Xaa Pro Ser Xaa His Leu
            95                  100                 105
Val Phe Met Arg Met Thr Pro Ser Ser Met Met Asn Thr Pro Ser Gly
        110                 115                 120
Asn Xaa Gly Cys Trp Ser Gln Leu Cys Cys Ser Ser Gln Ala Ser Ser
    125                 130                 135
Ser Ser Pro Val Ala Ser Ala Gly Ser Cys Pro Gly Tyr Ala Gly Ile
140                 145                 150                 155
Ile Ala Gly Glu Ser Ile Arg Asn Arg Ser
                160                 165
```

<210> 387
<211> 179
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 387
```
Met Glu Thr Gly Ala Leu Arg Arg Pro Gln Leu Leu Pro Leu Leu Leu
    -25                 -20                 -15
Leu Leu Cys Gly Pro Ser Gln Asp Gln Cys Arg Pro Val Leu Gln Asn
-10                 -5                  1                   5
Leu Leu Gln Ser Pro Gly Leu Thr Trp Ser Leu Glu Val Pro Thr Gly
            10                  15                  20
Arg Glu Gly Lys Glu Gly Gly Asp Arg Gly Pro Gly Leu Xaa Gly Ala
        25                  30                  35
Thr Pro Ala Arg Ser Pro Gln Gly Lys Glu Met Gly Arg Gln Arg Thr
    40                  45                  50
Arg Lys Val Lys Gly Pro Ala Trp Xaa His Thr Ala Asn Gln Glu Leu
55                  60                  65                  70
Asn Arg Met Arg Ser Leu Ser Ser Gly Ser Val Pro Val Gly His Leu
                75                  80                  85
Glu Gly Gly Thr Val Lys Leu Gln Lys Asp Thr Gly Leu His Ser Cys
            90                  95                  100
Xaa Asp Gly Met Ala Ser Leu Glu Gly Thr Pro Ala Ser Val Leu Ala
        105                 110                 115
Asp Ala Cys Pro Gly Phe His Asp Val Xaa Val Gln Xaa Ala Leu Phe
    120                 125                 130
Gly Leu Ser Gly Xaa Xaa Leu Trp Leu Lys Thr His Phe Cys Leu Ser
135                 140                 145                 150
Ile Xaa Leu
```

<210> 388
<211> 150
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -55..-1

<400> 388
```
Met Ala Thr Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys
-55                 -50                 -45                 -40
Tyr Tyr Arg Leu Cys Asp Lys Ala Glu Ala Trp Gly Ile Val Leu Glu
                -35                 -30                 -25
Thr Val Ala Thr Ala Gly Val Val Thr Ser Val Ala Phe Met Leu Thr
            -20                 -15                 -10
Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg Arg Lys Met
        -5                  1                   5
Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly Val Leu Gly Ile Phe Gly
10                  15                  20                  25
Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr Gly Pro Thr
                30                  35                  40
Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe Ser Cys Leu
            45                  50                  55
Leu Ala His Ala Val Ser Leu Thr Lys Leu Val Arg Gly Arg Lys Ala
        60                  65                  70
```

Pro Phe Pro Val Gly Asp Ser Gly Ser Gly Arg Gly Leu Gln Pro Ser
75 80 85
Pro Gly Cys Tyr Arg Tyr
90 95

<210> 389
<211> 236
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -31..-1

<400> 389
Met Leu Ser Lys Gly Leu Lys Arg Lys Arg Glu Glu Glu Glu Glu Lys
-30 -25 -20
Glu Pro Leu Ala Val Asp Ser Trp Trp Leu Asp Pro Gly His Ala Ala
-15 -10 -5 1
Val Ala Gln Ala Pro Pro Ala Val Ala Ser Ser Ser Leu Phe Asp Leu
5 10 15
Ser Val Leu Lys Leu His His Ser Leu Gln Xaa Ser Xaa Pro Asp Leu
20 25 30
Arg His Leu Val Leu Val Xaa Asn Thr Leu Arg Arg Ile Gln Ala Ser
35 40 45
Met Ala Pro Ala Ala Ala Leu Pro Pro Val Pro Thr Pro Pro Ala Ala
50 55 60 65
Pro Xaa Val Ala Asp Asn Leu Leu Ala Ser Ser Asp Ala Ala Leu Ser
70 75 80
Ala Ser Met Ala Xaa Leu Leu Glu Asp Leu Ser His Ile Glu Gly Leu
85 90 95
Ser Gln Ala Pro Gln Pro Leu Ala Asp Glu Gly Pro Pro Gly Arg Ser
100 105 110
Ile Gly Gly Xaa Pro Pro Xaa Leu Gly Ala Leu Asp Leu Leu Gly Pro
115 120 125
Ala Thr Gly Cys Leu Leu Asp Asn Gly Leu Glu Gly Leu Phe Glu Asp
130 135 140 145
Ile Asp Thr Ser Met Tyr Asp Asn Glu Leu Trp Ala Pro Ala Ser Glu
150 155 160
Gly Leu Lys Pro Gly Pro Glu Asp Gly Pro Gly Lys Glu Glu Ala Pro
165 170 175
Glu Leu Asp Glu Ala Glu Leu Asp Tyr Leu Met Asp Val Leu Val Gly
180 185 190
Thr Gln Ala Leu Glu Arg Pro Pro Gly Pro Gly Arg
195 200 205

<210> 390
<211> 149
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -100..-1

<400> 390
Met Glu Thr Leu Tyr Arg Val Pro Phe Leu Val Leu Glu Cys Pro Asn
-100 -95 -90 -85

Leu Lys Leu Lys Lys Pro Pro Trp Leu His Met Pro Ser Ala Met Thr
-80 -75 -70
Val Tyr Ala Leu Val Val Val Ser Tyr Phe Leu Ile Thr Gly Gly Ile
-65 -60 -55
Ile Tyr Asp Val Ile Val Glu Pro Pro Ser Val Gly Ser Met Thr Asp
-50 -45 -40
Glu His Gly His Gln Arg Pro Val Ala Phe Leu Ala Tyr Arg Val Asn
-35 -30 -25
Gly Gln Tyr Ile Met Glu Gly Leu Ala Ser Ser Phe Leu Phe Thr Met
-20 -15 -10 -5
Gly Gly Leu Gly Phe Ile Ile Leu Asp Gly Ser Asn Ala Pro Asn Ile
1 5 10
Pro Lys Leu Asn Arg Phe Leu Leu Leu Phe Ile Gly Phe Val Cys Val
15 20 25
Leu Xaa Ser Phe Xaa Xaa Ala Arg Val Phe Met Arg Met Lys Leu Pro
30 35 40
Gly Tyr Leu Met Gly
45

<210> 391
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -49..-1

<400> 391
Met Pro Phe His Phe Pro Phe Leu Gly Phe Val Cys Leu His Leu His
-45 -40 -35
Leu Thr Pro Cys Leu Thr Val Pro Arg Arg Pro Leu Phe Leu Leu Leu
-30 -25 -20
His Leu Cys Pro His Leu Pro Phe Leu Leu Leu Leu Ser Cys Val Gly
-15 -10 -5
Xaa Xaa Pro Ser Cys Leu Pro Ser Ser Ser Thr Cys Val Ser Leu His
1 5 10 15
Phe Phe Ile Pro Asp
20

<210> 392
<211> 241
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 392
Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg His Leu Gln Thr Asn
-30 -25 -20 -15
Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr Leu Ser Val
-10 -5 1
Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu Ala Val Thr
5 10 15
Ile Lys Cys Thr Phe Ser Ala Thr Gly Cys Pro Ser Glu Gln Pro Thr
20 25 30

Cys Leu Trp Phe Arg Tyr Gly Ala His Gln Pro Glu Asn Leu Cys Leu
35 40 45 50
Asp Gly Cys Lys Ser Glu Ala Xaa Lys Phe Thr Val Arg Glu Ala Leu
55 60 65
Lys Glu Asn Gln Val Ser Leu Thr Val Asn Arg Val Thr Ser Asn Asp
70 75 80
Ser Ala Ile Tyr Ile Cys Gly Ile Ala Phe Pro Ser Val Pro Glu Ala
85 90 95
Arg Ala Lys Gln Thr Gly Gly Gly Thr Thr Leu Val Val Arg Glu Ile
100 105 110
Lys Leu Leu Ser Lys Glu Leu Arg Ser Phe Leu Thr Ala Leu Val Ser
115 120 125 130
Leu Leu Ser Val Tyr Val Thr Gly Val Cys Val Ala Phe Ile Leu Leu
135 140 145
Ser Lys Ser Lys Ser Asn Pro Leu Arg Asn Lys Glu Ile Lys Glu Asp
150 155 160
Ser Gln Lys Lys Lys Ser Ala Arg Arg Ile Phe Gln Glu Ile Ala Gln
165 170 175
Glu Leu Tyr His Lys Arg His Val Glu Thr Asn Gln Gln Ser Glu Lys
180 185 190
Asp Asn Asn Thr Tyr Glu Asn Arg Arg Val Leu Ser Asn Tyr Glu Arg
195 200 205 210
Pro

<210> 393
<211> 47
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 393
Met Asn Cys Asn Val Val Ser Glu Arg Gly Lys Trp Leu Glu Val Glu
-30 -25 -20 -15
Cys Ser Leu Met Thr Cys Thr Thr Leu Ile Asn Ala Ser Ala Ile Ser
-10 -5 1
Thr Asn Thr Leu Thr Asp Met Gly Ser Phe Asp Arg Arg Glu Ser
5 10 15

<210> 394
<211> 65
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -28..-1

<400> 394
Met Ala Phe Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro
-25 -20 -15
Leu Gln Trp Ser Leu Leu Val Ala Val Val Ala Gly Ser Val Val Ser
-10 -5 1
Tyr Gly Val Thr Arg Val Glu Ser Glu Lys Cys Asn Asn Leu Trp Leu
5 10 15 20
Phe Leu Glu Thr Gly Gln Leu Pro Lys Asp Arg Ser Thr Asp Gln Xaa

```
                    25                  30                  35
Ser


<210> 395
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -24..-1

<400> 395
Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe Leu Ser Tyr Leu Pro
                -20                 -15                 -10
Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly Ser Thr Leu Gly Lys
            -5                  1                   5
Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg Pro Trp Asp Ala Ala
    10                  15                  20
Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Xaa Asn Xaa Tyr Xaa Xaa
25                  30                  35                  40
Trp Gly Gln Gly Thr His Ser Ser Leu
                45


<210> 396
<211> 60
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

<400> 396
Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro Thr
            -15                 -10                 -5
Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg Leu
        1                   5                   10
Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala Leu
15                  20                  25                  30
Gln Gly Thr Leu Thr Arg Leu Gln Ser Thr Pro Ala
                35                  40


<210> 397
<211> 192
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -93..-1

<400> 397
Met Ala Glu Leu Gly Leu Asn Glu His His Gln Asn Glu Val Ile Asn
            -90                 -85                 -80
Tyr Met Arg Phe Ala Arg Ser Lys Arg Gly Leu Arg Leu Lys Thr Val
```

```
        -75                          -70                          -65
Asp Ser Cys Phe Gln Asp Leu Lys Glu Ser Arg Leu Val Glu Asp Thr
    -60                     -55                     -50
Phe Thr Ile Asp Glu Val Ser Glu Val Leu Asn Gly Leu Gln Ala Val
-45                 -40                     -35                 -30
Val His Ser Glu Val Glu Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn
                -25                     -20                     -15
Val Leu Leu Leu Arg Gln Leu Phe Ala Gln Ala Glu Lys Trp Tyr Leu
            -10                     -5                      1
Lys Leu Gln Thr Asp Ile Ser Glu Leu Glu Asn Arg Glu Leu Leu Glu
    5                   10                  15
Gln Xaa Ala Glu Phe Glu Lys Ala Xaa Ile Thr Ser Ser Asn Lys Lys
20                  25                  30                      35
Pro Ile Leu Xaa Val Thr Xaa Pro Lys Leu Ala Pro Leu Asn Glu Gly
                40                  45                  50
Gly Thr Ala Lys Leu Leu Asn Lys Val Ile Cys Ile Ile Leu Arg Asn
            55                  60                  65
Gly Lys Ser Leu Ile Leu Ser Cys His Cys Leu Gly Trp Arg Asn Lys
        70                  75                  80
Ser Gly Arg Phe Val Ser Gly Pro Leu Arg Ile Ile Ser Pro Leu Gln
    85                  90                  95
```

<210> 398
<211> 149
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -72..-1

<400> 398

```
Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile Phe
        -70                 -65                 -60
Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala Leu
    -55                 -50                 -45
Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln Lys
-40                 -35                 -30                     -25
Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu Ala
                -20                 -15                 -10
Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His Ala
            -5                  1                   5
Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Ser Val
    10                  15                  20
Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala Pro Gly Pro Tyr
25                  30                  35                      40
Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro Val Ala Pro Gln
                45                  50                  55
His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys Asn Gln Lys Thr Leu
            60                  65                  70
Phe Ser Met Val Gly
        75
```

<210> 399
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 399
Met Thr Pro Leu Leu Thr Leu Ile Leu Val Val Leu Met Gly Leu Pro
-20 -15 -10 -5
Leu Ala Gln Ala Leu Asp Cys His Val Cys Ala Tyr Asn Gly Asp Asn
1 5 10
Cys Phe Asn Pro Met Arg Cys Pro Ala Met Val Ala Tyr Cys Met Thr
15 20 25
Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met Lys Val Ser Lys Ser Cys
30 35 40
Val Pro Arg Cys Phe Glu Xaa Cys Val
45 50

<210> 400
<211> 86
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 400
Met Asn Leu His Phe Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly
-20 -15 -10 -5
Leu Val Leu Ala Pro Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe
1 5 10
Pro Cys Ile Tyr Cys Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala
15 20 25
Phe Ser Phe Ile Thr Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu
30 35 40
Ile Leu Pro Glu Lys Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly
45 50 55 60
Pro Xaa Lys Leu Arg Gln
65

<210> 401
<211> 78
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 401
Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala Cys Gly Ser Leu Leu
-20 -15 -10
Pro Gly Leu Trp Gln His Leu Thr Ala Asn His Trp Pro Pro Phe Ser
-5 1 5 10
Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser Glu Gln Ile Ser Glu
15 20 25
Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Arg Ser Leu Asn Gln Glu
30 35 40
Pro Phe Val Ser Arg Ala Ile Arg Pro Lys Tyr Ser Ile Thr

45 50 55

<210> 402
<211> 65
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -28..-1

<400> 402
Met Gly Lys Gly His Gln Arg Pro Trp Trp Lys Val Leu Pro Leu Ser
-25 -20 -15
Cys Phe Leu Val Ala Leu Ile Ile Trp Cys Tyr Leu Arg Glu Glu Ser
-10 -5 1
Glu Ala Asp Gln Trp Leu Arg Gln Val Trp Gly Glu Val Pro Glu Pro
5 10 15 20
Ser Asp Arg Ser Glu Glu Pro Glu Thr Pro Ala Ala Tyr Arg Ala Arg
25 30 35
Thr

<210> 403
<211> 211
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -27..-1

<400> 403
Met Leu Leu Leu Ser Ile Thr Thr Ala Tyr Thr Gly Leu Glu Leu Thr
-25 -20 -15
Phe Phe Ser Gly Val Tyr Gly Thr Cys Ile Gly Ala Thr Asn Lys Phe
-10 -5 1 5
Gly Ala Glu Glu Xaa Ser Leu Ile Gly Leu Ser Gly Ile Phe Ile Gly
10 15 20
Ile Gly Glu Ile Leu Gly Gly Ser Leu Phe Gly Leu Leu Ser Lys Asn
25 30 35
Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile Leu Val His
40 45 50
Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly Asp Ala Pro
55 60 65
Ile Ala Pro Val Lys Gly Thr Asp Ser Ser Ala Tyr Ile Lys Ser Ser
70 75 80 85
Lys Xaa Phe Ala Ile Leu Cys Xaa Phe Leu Xaa Gly Leu Gly Asn Ser
90 95 100
Cys Phe Asn Thr Xaa Leu Leu Xaa Ile Xaa Gly Phe Leu Tyr Ser Glu
105 110 115
Xaa Ser Ala Pro Xaa Phe Ala Ile Phe Asn Phe Val Gln Ser Ile Cys
120 125 130
Ala Ala Val Ala Phe Phe Tyr Ser Asn Tyr Leu Leu Leu His Trp Gln
135 140 145
Leu Leu Val Met Val Ile Phe Gly Phe Xaa Gly Thr Ile Ser Phe Phe
150 155 160 165
Thr Val Glu Trp Glu Xaa Ala Ala Phe Val Xaa Arg Gly Ser Asp Tyr
170 175 180

Arg Ser Ile

<210> 404
<211> 123
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -80..-1

<400> 404
Met Ser Thr Trp Tyr Leu Ala Leu Asn Lys Ser Tyr Lys Asn Lys Asp
-80 -75 -70 -65
Ser Val Arg Ile Tyr Leu Ser Leu Cys Thr Val Ser Ile Lys Phe Thr
-60 -55 -50
Tyr Phe His Asp Ile Gln Thr Asn Cys Leu Thr Thr Trp Lys His Ser
-45 -40 -35
Arg Cys Arg Phe Tyr Trp Ala Phe Gly Gly Ser Ile Leu Gln His Ser
-30 -25 -20
Val Asp Pro Leu Val Leu Phe Leu Ser Leu Ala Leu Leu Val Thr Pro
-15 -10 -5
Thr Ser Thr Pro Ser Ala Lys Ile Gln Ser Leu Gln Ile Asp Leu Pro
1 5 10 15
Gly Gly Trp Arg Leu Ala Thr Asp Arg Ile Phe Thr Leu Ser Pro Val
20 25 30
Pro Met Asp Xaa Pro Leu Ile Leu His Gln Leu
35 40

<210> 405
<211> 86
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 405
Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp Leu Ile
-25 -20 -15
Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu Leu Pro
-10 -5 1 5
Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ile Ile Leu Leu Leu Leu
10 15 20
Ile Phe Ile Ser Ile Xaa Gly Ile Leu Tyr Lys Phe Xaa Asp Val Leu
25 30 35
Leu Tyr Phe Pro Xaa Gln Xaa Ser Ser Ser Arg Leu Tyr Asp Ser His
40 45 50
Ala His Trp Xaa Ser Xaa
55 60

<210> 406
<211> 162
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -31..-1

<400> 406
```
Met Ala Ala Ala Trp Pro Ser Gly Pro Xaa Ala Pro Glu Ala Val Thr
    -30                 -25                 -20
Ala Arg Leu Val Gly Val Leu Trp Phe Val Ser Val Thr Thr Gly Pro
-15                 -10                 -5                  1
Trp Gly Ala Val Ala Thr Ser Ala Gly Gly Glu Glu Ser Leu Lys Cys
            5                   10                  15
Glu Asp Leu Lys Val Gly Gln Tyr Ile Cys Lys Asp Pro Lys Ile Asn
        20                  25                  30
Asp Ala Thr Gln Glu Pro Val Asn Cys Thr Asn Tyr Thr Ala His Val
    35                  40                  45
Ser Cys Phe Pro Ala Pro Asn Ile Thr Cys Lys Asp Ser Ser Gly Asn
50                  55                  60                  65
Glu Thr His Phe Thr Gly Asn Glu Val Gly Phe Phe Lys Pro Ile Ser
                70                  75                  80
Cys Arg Asn Val Asn Gly Tyr Ser Tyr Asn Glu Gln Ser His Val Ser
            85                  90                  95
Phe Ser Trp Met Val Gly Ser Arg Ser Ile Leu Pro Trp Ile Pro Cys
        100                 105                 110
Phe Gly Phe Val Lys Xaa Xaa His Cys Arg Val Xaa Trp Asn Trp Glu
    115                 120                 125
Pro Asn
130
```

<210> 407
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -37..-1

<400> 407
```
Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile
        -35                 -30                 -25
Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe
    -20                 -15                 -10
Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu
-5                  1                   5                   10
Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Xaa Gln
            15                  20                  25
Xaa Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly
        30                  35                  40
Gly Phe Ser Phe Cys Gln Xaa Arg Leu Asn Lys Arg Lys Glu Tyr Met
    45                  50                  55
Val Arg
60
```

<210> 408
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 408
Met Arg Phe Leu Pro Cys Cys Leu Leu Trp Ser Val Phe Asn Pro Glu
-15 -10 -5 1
Ser Leu Asn Cys His Tyr Phe Xaa Xaa Glu Xaa Cys Ile Phe Xaa Ser
5 10 15
Leu Gln Tyr Tyr Glu Ile Ser Leu Gln Glu Lys Leu Leu Gly Phe Leu
20 25 30
Trp Leu Cys Phe Leu Ser Tyr Phe Phe Arg Ala Val Tyr Phe Leu Ile
35 40 45
Asp Phe Ser Ser Phe Thr
50 55

<210> 409
<211> 60
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -45..-1

<400> 409
Met His Ser Leu Phe Ile Ala Ser Leu Lys Val Leu Phe Tyr Tyr Ser
-45 -40 -35 -30
Phe Ser Phe Arg Phe Asn Trp Phe Asp Cys Leu Leu His Asn Leu Gly
-25 -20 -15
Glu Asn Phe Leu Ser Leu Leu Ser Lys Ser Cys Ser Ala Asp Pro Ser
-10 -5 1
Gly Ser Thr Phe Met Arg Asp Ile Glu Thr Asn Lys
5 10 15

<210> 410
<211> 39
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -22..-1

<400> 410
Met Pro Glu Ala Val Glu Gln Ser Ala His Leu Phe Val Thr Trp Ser
-20 -15 -10
Ser Gln Arg Ala Leu Ser His Pro Ala Pro Phe Leu Thr Xaa Xaa Lys
-5 1 5 10
Asn Pro Phe Leu Trp Lys Leu
15

<210> 411
<211> 51
<212> PRT

<213> Homo sapiens

<220>
<221> SIGNAL
<222> -23..-1

<400> 411
Met Ala Phe Gln Ser Leu Leu Glu Met Lys Phe Phe Leu Cys Ala Ala
-20 -15 -10
Phe Pro Leu Gly Ala Gly Val Lys Met Phe His Tyr Leu Gly Pro Gly
-5 1 5
Lys Pro Leu Xaa Gln Ala Ser Pro Ser Pro His Pro His Arg Xaa Arg
10 15 20 25
Ile Trp Pro

<210> 412
<211> 95
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -48..-1

<400> 412
Met Ala Ser Ser His Trp Asn Glu Thr Thr Thr Ser Val Tyr Gln Tyr
-45 -40 -35
Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro Phe His Asp Asn Trp Asn
-30 -25 -20
Thr Ala Cys Phe Val Ile Leu Leu Leu Phe Ile Phe Thr Val Val Ser
-15 -10 -5
Leu Val Val Leu Ala Phe Leu Tyr Glu Val Leu Xaa Xaa Cys Cys Cys
1 5 10 15
Val Lys Asn Lys Thr Val Lys Asp Leu Lys Ser Glu Pro Asn Pro Leu
20 25 30
Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg Glu Thr Glu Val Val
35 40 45

<210> 413
<211> 60
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -32..-1

<400> 413
Met Asp Glu Tyr Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly
-30 -25 -20
Gln Met Phe Thr Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys
-15 -10 -5
Gln Arg Phe Phe Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser
1 5 10 15
Thr Val Thr Pro Ser Trp Arg Leu Cys Leu Val Ser
20 25

<210> 414
<211> 170
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -79..-1

<400> 414
Met Glu Asp Pro Asn Pro Glu Glu Asn Met Lys Gln Gln Asp Ser Pro
-75 -70 -65
Lys Glu Arg Ser Pro Gln Ser Pro Gly Gly Asn Ile Cys His Leu Gly
-60 -55 -50
Ala Pro Lys Cys Thr Arg Cys Leu Ile Thr Phe Ala Asp Ser Lys Phe
-45 -40 -35
Gln Glu Arg His Met Lys Arg Glu His Pro Ala Asp Phe Val Ala Gln
-30 -25 -20
Lys Leu Gln Gly Val Leu Phe Ile Cys Phe Thr Cys Ala Arg Ser Phe
-15 -10 -5 1
Pro Ser Ser Lys Ala Xaa Xaa Thr His Gln Arg Ser His Gly Pro Xaa
5 10 15
Ala Lys Pro Thr Leu Pro Val Ala Thr Thr Thr Ala Gln Pro Thr Phe
20 25 30
Pro Cys Pro Asp Cys Gly Lys Thr Phe Gly Gln Ala Val Ser Leu Xaa
35 40 45
Arg His Xaa Gln Xaa His Glu Val Arg Ala Pro Pro Gly Thr Phe Ala
50 55 60 65
Cys Thr Xaa Cys Gly Gln Asp Phe Ala Gln Glu Xaa Gly Leu His Gln
70 75 80
His Tyr Ile Arg His Ala Arg Gly Gly Leu
85 90

<210> 415
<211> 190
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -82..-1

<400> 415
Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe
-80 -75 -70
His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly
-65 -60 -55
Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val Ile
-50 -45 -40 -35
Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln
-30 -25 -20
Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr
-15 -10 -5
Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile
1 5 10
Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Xaa Phe Glu Asp Ile
15 20 25 30
Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln Leu
35 40 45

Trp Ser Thr Tyr Gln Val Arg Xaa Ala Asp Trp Ser Leu Glu Ala Leu
50 55 60
Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser Phe
65 70 75
Asp Ala Asp Lys Glu Xaa Ile Ala Glu Ser Thr Leu Pro Gly Arg His
80 85 90
Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu
95 100 105

<210> 416
<211> 114
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -60..-1

<400> 416
Met Met Ala Ala Val Pro Pro Gly Leu Glu Pro Trp Asn Arg Val Arg
-60 -55 -50 -45
Ile Pro Lys Ala Gly Asn Arg Ser Ala Val Thr Val Gln Asn Pro Gly
-40 -35 -30
Ala Ala Leu Asp Leu Cys Ile Ala Ala Val Ile Lys Glu Cys His Leu
-25 -20 -15
Val Ile Leu Ser Leu Lys Ser Gln Thr Leu Asp Ala Glu Thr Asp Val
-10 -5 1
Leu Cys Ala Val Leu Tyr Ser Asn His Asn Arg Met Gly Arg His Lys
5 10 15 20
Pro His Leu Ala Leu Lys Gln Val Glu Gln Cys Leu Lys Arg Leu Lys
25 30 35
Asn Met Asn Leu Glu Gly Ser Ile Gln Asp Leu Phe Glu Leu Phe Ser
40 45 50
Ser Lys

<210> 417
<211> 161
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -108..-1

<400> 417
Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln Ser Pro Gln Ala Leu
-105 -100 -95
Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser Ile Thr Leu Thr Leu
-90 -85 -80
Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg Asn Val Thr His Leu
-75 -70 -65
Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu Ser Gly Arg Glu Ala
-60 -55 -50 -45
His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro Thr Ala Trp Ser Ser
-40 -35 -30
Asp Asp Cys Ala Leu His Gly His Cys Glu Gln Val Val Phe Thr Ala
-25 -20 -15
Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe Pro Ser Leu Tyr Ser

```
        -10                 -5                  1
His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr Pro Arg Ser Gly Thr
5                   10                  15                  20
Arg Ser Ser Gln Leu Pro Glu Met Pro Thr Gln Asn Thr Pro Lys Ile
                25                  30                  35
Thr Ile Leu Ser Gly Val Ile Arg Gly Pro Leu Glu Lys Ser Ile Met
            40                  45                  50
Leu
```

<210> 418
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 418

```
Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu
    -20                 -15                 -10
Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val
-5                  1                   5                   10
Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val
            15                  20                  25
Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro
        30                  35                  40
Leu Arg Met
    45
```

<210> 419
<211> 332
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -32..-1

<400> 419

```
Met Ile Xaa Leu Arg Asp Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp
        -30                 -25                 -20
Thr Arg Gln Leu Pro Leu Leu Thr Ser Ala Leu His Gly Leu Gln Gln
    -15                 -10                 -5
Gln His Pro Ala Phe Ser Gly Val Ala Arg Leu Ala Lys Arg Trp Val
1               5                   10                  15
Arg Ala Gln Leu Leu Gly Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu
            20                  25                  30
Val Ala Ala Ala Leu Phe Leu His Pro Glu Pro Phe Thr Pro Pro Ser
        35                  40                  45
Ser Pro Gln Val Gly Phe Leu Arg Phe Leu Phe Leu Val Ser Thr Phe
    50                  55                  60
Asp Trp Lys Asn Asn Pro Leu Phe Val Asn Leu Asn Asn Glu Leu Thr
65                  70                  75                  80
Val Glu Glu Gln Val Glu Ile Arg Ser Gly Phe Leu Ala Ala Arg Ala
                85                  90                  95
Gln Leu Pro Val Met Val Ile Val Thr Pro Gln Xaa Arg Lys Asn Ser
            100                 105                 110
```

Val Trp Thr Gln Asp Gly Pro Ser Ala Gln Ile Leu Gln Gln Leu Val
115 120 125
Val Leu Ala Ala Glu Xaa Leu Pro Met Leu Xaa Xaa Gln Leu Met Asp
130 135 140
Pro Arg Gly Pro Gly Asp Ile Arg Thr Xaa Phe Arg Pro Pro Leu Asp
145 150 155 160
Ile Tyr Asp Val Leu Ile Arg Leu Ser Pro Arg His Ile Pro Arg His
165 170 175
Arg Gln Ala Val Asp Ser Pro Ala Ala Ser Phe Cys Arg Gly Leu Leu
180 185 190
Ser Gln Pro Gly Pro Ser Ser Leu Met Pro Val Leu Gly Xaa Asp Pro
195 200 205
Pro Gln Leu Tyr Leu Thr Gln Leu Xaa Glu Ala Phe Gly Asp Leu Ala
210 215 220
Leu Phe Phe Tyr Asp Gln His Gly Gly Glu Val Ile Gly Val Leu Trp
225 230 235 240
Lys Pro Thr Ser Phe Gln Pro Gln Pro Phe Lys Ala Ser Ser Thr Lys
245 250 255
Gly Arg Met Val Met Ser Arg Gly Gly Glu Leu Val Met Val Pro Asn
260 265 270
Val Glu Ala Ile Leu Glu Asp Phe Ala Val Leu Gly Glu Gly Leu Val
275 280 285
Gln Thr Val Glu Ala Arg Ser Glu Arg Trp Thr Val
290 295 300

<210> 420
<211> 65
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -19..-1

<400> 420
Met Gly Gly Ile Trp Asn Ala Leu Ser Met Ser Ser Phe Ser Phe His
-15 -10 -5
Ser Ser Ser Cys Ser Ala Leu Ser Ala Lys Ser Leu Leu Ser Arg His
1 5 10
His Ile Leu Gln Gln Phe Leu Val Arg Lys Ser Val Pro Leu Glu Asn
15 20 25
Ala Ser Leu Pro Phe Pro His Leu Gly Ser Ser Leu Phe Lys Ile Val
30 35 40 45
Gly

<210> 421
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 421
Met Pro Thr Gly Lys Gln Leu Ala Asp Ile Gly Tyr Lys Thr Phe Ser
-30 -25 -20 -15
Thr Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val

```
                -10                 -5                  1
Arg Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Gln Ala Ala
        5                   10                  15
Glu Glu Gln Lys Xaa Ser Gly Ile Met
    20                  25
```

<210> 422
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 422

```
Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val
        -15                 -10                 -5
Gly Phe Pro Val Ser Gln Asp Gln Glu Arg Glu Lys Arg Ser Ile Ser
    1               5                   10                  15
Asp Ser Asp Glu Leu Ala Ser Gly Xaa Phe Val Phe Pro Tyr Pro Tyr
                20                  25                  30
Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe
            35                  40                  45
Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro
        50                  55                  60
Leu Pro Ser Glu Lys
    65
```

<210> 423
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 423

```
Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val
        -15                 -10                 -5
Gly Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser
    1               5                   10                  15
Asp Ser Asp Glu Leu Ala Ser Gly Phe Phe Val Phe Pro Tyr Pro Tyr
                20                  25                  30
Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe
            35                  40                  45
Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro
        50                  55                  60
Leu Pro Ser Glu Lys
    65
```

<210> 424
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -29..-1

<400> 424
Met Thr Cys Arg Gly Ser Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser
-25 -20 -15
Glu Leu Ser Leu Leu Pro Ser Ser Leu Trp Val Leu Ala Thr Ser Ser
-10 -5 1
Pro Thr Ile Thr Ile Ala Leu Ala Met Ala Ala Gly Asn Leu Cys Pro
5 10 15
Leu Pro Ser Ser Xaa Arg Xaa Lys Arg Arg Trp Cys Gln Ala Xaa Gln
20 25 30 35
Gln Xaa Ala Leu Leu
40

<210> 425
<211> 122
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -56..-1

<400> 425
Met Val Pro Trp Pro Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Ile
-55 -50 -45
Ser Arg Phe Pro Phe Leu Pro Thr His Asp Pro Pro Thr Pro Ala His
-40 -35 -30 -25
Trp Ser Pro Ala Ser His Gln Gln Phe Lys His Xaa Ser Pro Leu Leu
-20 -15 -10
Thr Leu Ala Leu Leu Gly Gln Cys Ser Leu Phe Xaa Asn Leu Arg Lys
-5 1 5
Lys Leu Ala Gly Gln Lys Ala Lys Lys Leu Pro Ser Phe Ser Ser Leu
10 15 20
Pro Leu Thr Leu Trp Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr
25 30 35 40
Val Ala Gln Lys Lys Leu Arg Trp Ser Gly Thr Leu Gly Trp Gly Pro
45 50 55
Val Pro Ser Trp Val Gln Phe Phe Leu Gly
60 65

<210> 426
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 426
Met Ala Cys Glu Thr His Gly Val Leu Val Pro Ala His Leu Ser Gly
-30 -25 -20 -15
Leu Ile Thr Cys Leu Leu Ala Phe Trp Val Pro Ala Ser Cys Ile Gln
-10 -5 1

```
Arg Cys Ser Gly Ser Pro Leu Pro Leu
        5                   10



<210> 427
<211> 50
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -36..-1

<400> 427
Met Ala Pro His Thr Ala Ser Phe Gly Val Cys Pro Leu Leu Ser Val
    -35                 -30                 -25
Thr Arg Val Val Ala Thr Glu His Trp Leu Phe Leu Ala Ser Leu Ser
-20                 -15                 -10                 -5
Gly Ile Lys Thr Tyr Gln Ser Tyr Ile Ser Val Phe Cys Lys Val Thr
                1                   5                   10
Leu Ile



<210> 428
<211> 136
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

<400> 428
Met Asp Ser Leu Arg Lys Met Leu Ile Ser Val Ala Met Leu Gly Ala
            -15                 -10                 -5
Xaa Ala Gly Val Gly Tyr Ala Leu Leu Val Ile Val Thr Pro Gly Glu
        1                   5                   10
Arg Arg Lys Gln Glu Met Leu Lys Glu Met Pro Leu Gln Asp Pro Arg
15                  20                  25                  30
Ser Arg Glu Glu Ala Ala Arg Thr Gln Gln Leu Leu Leu Ala Thr Leu
                35                  40                  45
Gln Glu Ala Ala Thr Thr Gln Glu Asn Val Ala Trp Arg Lys Asn Trp
            50                  55                  60
Met Val Gly Gly Glu Gly Gly Ala Thr Gly Xaa His Arg Glu Thr Gly
        65                  70                  75
Leu Ala Ser Val Gly Ala Gly Pro Trp Leu Gly Arg Arg Asn Pro Arg
    80                  85                  90
Gln Leu Ser Pro Ser Trp Ala Xaa Arg Lys Ile Arg Xaa Glu Asn Xaa
95                  100                 105                 110
Met Pro Gly Leu Ser Gly Val Leu
                115



<210> 429
<211> 194
<212> PRT
<213> Homo sapiens

<220>
```

<221> SIGNAL
<222> -65..-1

<400> 429

```
Met Gln Asp Ala Pro Leu Ser Cys Leu Ser Pro Thr Lys Trp Ser Ser
-65                 -60                 -55                 -50
Val Ser Ser Ala Asp Ser Thr Glu Lys Ser Ala Ser Ala Ala Gly Thr
                -45                 -40                 -35
Arg Asn Leu Pro Phe Gln Phe Cys Leu Arg Gln Ala Leu Arg Met Lys
            -30                 -25                 -20
Ala Ala Gly Ile Leu Thr Leu Ile Gly Cys Leu Val Thr Gly Val Glu
        -15                 -10                 -5
Ser Lys Ile Tyr Thr Arg Cys Lys Leu Ala Lys Ile Phe Ser Arg Ala
    1               5                   10                  15
Gly Leu Asp Asn Xaa Arg Gly Phe Ser Leu Gly Asn Trp Ile Cys Met
                20                  25                  30
Ala Tyr Tyr Glu Ser Gly Tyr Asn Thr Thr Ala Gln Thr Val Leu Asp
            35                  40                  45
Asp Gly Ser Ile Asp Tyr Gly Ile Phe Gln Ile Asn Ser Phe Ala Trp
        50                  55                  60
Cys Arg Arg Gly Lys Leu Lys Glu Asn Asn His Cys His Val Ala Cys
    65                  70                  75
Ser Ala Leu Xaa Thr Asp Asp Leu Thr Asp Ala Ile Ile Cys Ala Xaa
80                  85                  90                  95
Lys Ile Val Lys Glu Thr Gln Gly Met Asn Tyr Trp Gln Gly Trp Lys
                100                 105                 110
Lys His Cys Glu Gly Arg Asp Leu Ser Xaa Trp Lys Lys Gly Cys Glu
            115                 120                 125
Val Ser
```

<210> 430
<211> 141
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -69..-1

<400> 430

```
Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser
                -65                 -60                 -55
Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln
            -50                 -45                 -40
Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Ile Lys Val Ile
        -35                 -30                 -25
Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile
    -20                 -15                 -10
Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser
-5                  1               5                   10
Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Val Xaa
            15                  20                  25
Lys Xaa Ser Glu Glu Gly Arg Met Gly Gln Xaa Gly Glu Glu Xaa Xaa
        30                  35                  40
Asn Ser Leu Asn Phe Pro Xaa Ala Ser Leu Leu Xaa Leu Ile Cys Gln
    45                  50                  55
Xaa Gln Gly Phe Asn Gly Glu Ser Cys Ser Pro Val Gly
60                  65                  70
```

<210> 431
<211> 248
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -69..-1

<400> 431
```
Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser
                -65                 -60                 -55
Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln
            -50                 -45                 -40
Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Xaa Lys Val Ile
        -35                 -30                 -25
Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile
    -20                 -15                 -10
Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser
-5                  1               5                   10
Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Phe Ile
            15                  20                  25
Ile Ser Gly Ser Leu Ser Ile Ala Thr Lys Lys Arg Leu Thr Asn Leu
        30                  35                  40
Leu Val His Thr Thr Leu Val Gly Ser Ile Leu Ser Ala Leu Ser Ala
    45                  50                  55
Leu Val Gly Phe Ile Xaa Leu Ser Val Lys Gln Ala Thr Leu Asn Pro
60                  65                  70                  75
Ala Ser Leu Xaa Cys Glu Leu Xaa Lys Asn Asn Ile Pro Thr Xaa Xaa
                80                  85                  90
Tyr Val Xaa Tyr Phe Tyr His Asp Ser Leu Tyr Thr Thr Asp Xaa Tyr
            95                  100                 105
Thr Ala Lys Ala Xaa Leu Ala Gly Thr Leu Ser Leu Met Leu Ile Cys
        110                 115                 120
Thr Leu Leu Glu Phe Cys Xaa Xaa Val Leu Thr Ala Val Leu Arg Trp
    125                 130                 135
Lys Gln Ala Tyr Ser Asp Phe Pro Gly Ser Val Leu Phe Leu Pro Xaa
140                 145                 150                 155
Ser Tyr Ile Gly Asn Ser Gly Met Ser Ser Lys Met Thr His Asp Cys
                160                 165                 170
Gly Tyr Glu Glu Leu Leu Thr Ser
            175
```

<210> 432
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -36..-1

<400> 432
```
Met Gln Val Pro His Leu Arg Val Trp Thr Gln Val Xaa Asp Thr Phe
    -35                 -30                 -25
Ile Gly Tyr Arg Asn Leu Gly Phe Thr Ser Met Cys Ile Leu Phe His
-20                 -15                 -10                 -5
Cys Leu Leu Ser Phe Gln Val Phe Lys Lys Lys Arg Lys Leu Xaa Leu
                1               5                   10
```

Phe

<210> 433
<211> 86
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -14..-1

<400> 433

```
Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp Cys
                -10                 -5                   1
Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Leu Arg Ser Ser Ala
        5                   10                  15
Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly Trp
    20                  25                  30
Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg Leu
35                  40                  45                  50
Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu Gly
                55                  60                  65
His Arg Ile Cys Asp Leu
            70
```

<210> 434
<211> 144
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -58..-1

<400> 434

```
Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile
            -55                 -50                 -45
Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro
        -40                 -35                 -30
Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu
    -25                 -20                 -15
Asp Ser Val Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val
-10                 -5                   1               5
Phe Ser Thr Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe Leu
            10                  15                  20
Thr Phe Asp Leu Leu His Arg Pro Ala Val Thr Leu Cys His Ser Ala
        25                  30                  35
Asn Phe Ser Pro Gly Ala Arg Val Arg Gly Pro Val Lys Val Leu Asp
    40                  45                  50
Ser Arg Arg Leu Tyr Ser Cys Lys Trp Val Gln Ser Gln Asp Asn Leu
55                  60                  65                  70
Ala Ser Arg Lys His Cys Cys Cys Cys Ser Trp Gly Trp Ala Arg Ser
                75                  80                  85
```

<210> 435
<211> 121

```
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 435
Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala
    -15                 -10                 -5
Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln
1               5                   10                  15
Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser
            20                  25                  30
Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Ser
        35                  40                  45
Glu Ser Pro Pro Gly Arg Gly Xaa Val Pro Xaa Ala Gly Glu Xaa Pro
    50                  55                  60
Val Pro Pro Pro Leu Xaa Asp Leu Xaa Met Thr Pro Arg Xaa Xaa Arg
65                  70                  75                  80
Ala Trp Gly Pro Val Gly Pro Lys Val Pro Pro Ala Val Ser Pro Ala
                85                  90                  95
Leu Gly Ser Gly Glu His Pro Xaa Xaa
            100                 105


<210> 436
<211> 162
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 436
Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala
    -15                 -10                 -5
Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln
1               5                   10                  15
Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser
            20                  25                  30
Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Lys
        35                  40                  45
Trp Ser Val Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro
    50                  55                  60
Asn Asp Asn Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly
65                  70                  75                  80
Val Ile Thr Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu
                85                  90                  95
Thr Pro Gln Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Leu Gln
            100                 105                 110
Asp Pro Ser Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu
        115                 120                 125
Pro Leu Cys Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln
    130                 135                 140
Glu Gly
145
```

<210> 437
<211> 110
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -20..-1

<400> 437
Met Xaa Leu Met Val Leu Val Phe Thr Ile Gly Leu Thr Leu Leu Leu
-20 -15 -10 -5
Gly Xaa Gln Ala Met Pro Ala Asn Arg Leu Ser Cys Tyr Arg Lys Ile
1 5 10
Leu Lys Asp His Asn Cys His Asn Leu Pro Glu Gly Val Ala Asp Leu
15 20 25
Thr Gln Ile Asp Val Asn Val Gln Asp His Phe Trp Asp Gly Lys Gly
30 35 40
Cys Glu Met Ile Cys Tyr Cys Asn Phe Lys Arg Ile Ala Leu Leu Pro
45 50 55 60
Lys Arg Arg Phe Leu Trp Thr Lys Asp Leu Phe Arg Asp Ser Leu Gln
65 70 75
Gln Ser Met Arg Ile Phe Met Tyr Ser Gly Glu His His Ser
80 85 90

<210> 438
<211> 71
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 438
Met Lys Leu Leu Thr His Asn Leu Leu Ser Ser His Val Arg Gly Val
-15 -10 -5 1
Gly Ser Arg Gly Phe Pro Leu Arg Leu Gln Ala Thr Glu Val Arg Ile
5 10 15
Cys Pro Val Glu Phe Asn Pro Asn Phe Val Ala Arg Met Ile Pro Lys
20 25 30
Val Glu Trp Ser Ala Phe Leu Glu Ala Xaa Asp Asn Leu Arg Leu Ile
35 40 45
Gln Val Pro Arg Arg Ala Gly
50 55

<210> 439
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -24..-1

<400> 439
Met Lys Ser Ala Lys Leu Gly Phe Leu Leu Arg Phe Phe Ile Phe Cys
-20 -15 -10

Ser Leu Asn Thr Leu Leu Leu Gly Gly Val Asn Lys Ile Ala Glu Lys
-5 1 5
Ile Cys Gly Asp Leu Lys Asp Pro Cys Lys Leu Asp Met Asn Phe Gly
10 15 20
Ser Cys Tyr Glu Val His Phe Arg Tyr Phe Tyr Asn Arg Thr Ser Lys
25 30 35 40
Arg Cys Glu Thr Phe Val Phe Ser Ser Cys Asn Gly Asn Leu Asn Asn
45 50 55
Phe Lys Leu Lys Ile Glu Arg Glu Val Xaa Cys Val Ala Lys Tyr Lys
60 65 70
Pro Pro Arg
75

<210> 440
<211> 169
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -25..-1

<400> 440
Met Arg Lys Pro Ala Ala Gly Phe Leu Pro Ser Leu Leu Lys Val Leu
-25 -20 -15 -10
Leu Leu Pro Leu Ala Pro Ala Ala Ala Gln Asp Ser Thr Gln Ala Ser
-5 1 5
Thr Pro Gly Ser Pro Leu Ser Pro Thr Glu Tyr Gln Arg Phe Phe Ala
10 15 20
Leu Leu Thr Pro Thr Trp Lys Ala Glu Thr Thr Cys Arg Leu Arg Ala
25 30 35
Thr His Gly Cys Arg Asn Pro Thr Leu Val Gln Leu Asp Gln Tyr Glu
40 45 50 55
Asn His Gly Leu Val Pro Asp Gly Ala Val Cys Ser Asn Leu Pro Tyr
60 65 70
Ala Ser Trp Phe Glu Ser Phe Cys Gln Phe Thr His Tyr Arg Cys Ser
75 80 85
Asn His Val Tyr Tyr Ala Lys Arg Val Leu Cys Ser Gln Pro Val Ser
90 95 100
Ile Leu Ser Pro Asn Thr Leu Lys Glu Ile Glu Xaa Ser Ala Glu Val
105 110 115
Ser Pro Thr Thr Asp Asp Leu Pro His Leu Thr Pro Leu His Ser Asp
120 125 130 135
Arg Thr Pro Asp Leu Pro Ala Leu Ala
140

<210> 441
<211> 167
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -76..-1

<400> 441
Met Gly Asp Tyr Leu Leu Arg Gly Tyr Arg Met Leu Gly Glu Thr Cys
-75 -70 -65

```
Ala Asp Cys Gly Thr Ile Leu Leu Gln Asp Lys Gln Arg Lys Ile Tyr
-60                 -55                 -50                 -45
Cys Val Ala Cys Gln Glu Leu Asp Ser Asp Val Asp Lys Asp Asn Pro
                -40                 -35                 -30
Ala Leu Asn Ala Gln Ala Ala Leu Ser Gln Ala Arg Glu His Gln Leu
            -25                 -20                 -15
Ala Ser Ala Ser Glu Leu Pro Leu Gly Ser Arg Pro Ala Pro Gln Pro
        -10                 -5                  1
Pro Val Pro Arg Pro Glu His Cys Glu Gly Ala Ala Ala Gly Leu Lys
5                   10                  15                  20
Ala Ala Gln Gly Pro Pro Ala Pro Ala Val Pro Pro Asn Thr Xaa Val
                25                  30                  35
Met Ala Cys Thr Gln Thr Ala Leu Leu Gln Lys Leu Thr Trp Ala Ser
            40                  45                  50
Ala Glu Leu Gly Ser Xaa Thr Ser Xaa Gly Lys Xaa Ala Ser Ser Cys
        55                  60                  65
Val Ala Leu Ser Ala His Val Arg Arg Pro Cys Ala Ala Cys Ser Ser
    70                  75                  80
Tyr Ser Thr Lys Arg Ser Pro
85                  90
```

```
<210> 442
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 442
Met Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg
-15                 -10                 -5                  1
Gln Ile Gln Val Leu Lys Met Leu Pro Arg Glu Lys Leu Arg Arg Arg
            5                   10                  15
Glu Glu Arg Lys Gln Ile Asn Gly Lys Lys Xaa Arg Thr Lys Tyr Glu
        20                  25                  30
Thr Pro Arg Lys Xaa Xaa Gly Lys Lys Gly Gly Asn Xaa Xaa Xaa Xaa
    35                  40                  45
Xaa Leu Ser Lys Arg Asp
50                  55
```

```
<210> 443
<211> 381
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -33..-1

<400> 443
Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln Arg Val Ser Ser
            -30                 -25                 -20
Val Gly Ala Asn Xaa Leu Cys Leu Gly Met Ala Leu Cys Pro Arg Gln
        -15                 -10                 -5
Ala Thr Arg Ile Pro Leu Asn Gly Thr Trp Leu Phe Thr Pro Val Ser
    1                   5                   10                  15
```

```
Lys Met Ala Thr Val Lys Ser Glu Leu Ile Glu Arg Phe Thr Ser Glu
                20                  25                  30
Lys Pro Val His His Ser Lys Val Ser Ile Ile Gly Thr Gly Ser Val
            35                  40                  45
Gly Met Ala Cys Ala Ile Ser Ile Leu Leu Lys Gly Leu Ser Asp Glu
        50                  55                  60
Leu Ala Leu Val Asp Leu Asp Glu Xaa Lys Leu Lys Gly Glu Thr Met
    65                  70                  75
Asp Leu Gln His Gly Ser Pro Phe Thr Lys Met Pro Asn Ile Val Cys
80                  85                  90                  95
Ser Lys Xaa Tyr Phe Val Thr Ala Asn Ser Asn Leu Val Ile Ile Thr
                100                 105                 110
Ala Gly Ala Arg Gln Xaa Lys Gly Glu Thr Arg Leu Asn Leu Xaa Gln
            115                 120                 125
Arg Asn Val Ala Ile Phe Lys Leu Met Ile Ser Ser Ile Val Gln Tyr
        130                 135                 140
Ser Pro His Cys Lys Leu Ile Ile Val Ser Asn Pro Val Asp Ile Leu
    145                 150                 155
Thr Tyr Val Ala Trp Lys Leu Ser Ala Phe Pro Lys Asn Arg Ile Ile
160                 165                 170                 175
Gly Ser Gly Cys Asn Leu Ile Xaa Ala Arg Phe Arg Phe Leu Ile Gly
                180                 185                 190
Gln Lys Leu Gly Ile His Ser Glu Ser Cys His Gly Trp Ile Leu Gly
            195                 200                 205
Glu His Gly Asp Ser Ser Val Pro Val Trp Ser Gly Val Asn Ile Ala
        210                 215                 220
Gly Val Pro Leu Lys Asp Leu Asn Ser Asp Ile Gly Thr Asp Lys Asp
    225                 230                 235
Pro Glu Gln Trp Lys Asn Val His Lys Glu Val Thr Ala Thr Ala Tyr
240                 245                 250                 255
Glu Ile Ile Lys Met Lys Gly Tyr Thr Ser Trp Ala Ile Gly Leu Ser
                260                 265                 270
Val Ala Asp Leu Thr Glu Ser Ile Leu Lys Asn Leu Arg Arg Ile His
            275                 280                 285
Pro Val Ser Thr Ile Thr Lys Gly Leu Tyr Gly Ile Xaa Glu Glu Val
        290                 295                 300
Phe Leu Ser Ile Pro Cys Ile Leu Gly Glu Asn Gly Ile Thr Asn Leu
    305                 310                 315
Ile Lys Ile Lys Leu Thr Pro Glu Glu Glu Ala His Leu Lys Lys Ser
320                 325                 330                 335
Ala Lys Thr Leu Trp Glu Ile Gln Asn Lys Leu Lys Leu
                340                 345
```

<210> 444
<211> 39
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -14..-1

<400> 444

```
Met Tyr Tyr Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His
                -10                 -5                  1
Leu Pro Ile Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr
        5                   10                  15
Val Tyr Pro Thr Ser Ala Gly
    20                  25
```

<210> 445
<211> 50
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -37..-1

<400> 445
Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
-35 -30 -25
Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
-20 -15 -10
Ser Pro Cys Leu Thr Ala Pro Lys Ser Pro Arg Leu Ala Met Met Pro
-5 1 5 10
Asp Asn

<210> 446
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 446
Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg Pro Leu Ala Ser
-25 -20 -15
Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser Gly Ser His Trp
-10 -5 1 5
Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser Leu Ser Ala Thr
10 15 20
Thr Arg Gly
25

<210> 447
<211> 242
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 447
Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val
-30 -25 -20 -15
Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Ala Pro
-10 -5 1
Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu
5 10 15
Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu
20 25 30
Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly

35 40 45 50
Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly
55 60 65
Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Met Thr Asp Asn
70 75 80
Lys Thr Gly Glu Val Leu Ile Ser Glu Asn Val Val Ala Ser Ile Gln
85 90 95
Pro Xaa Glu Gly Xaa Phe Glu Gly Asp Leu Lys Val Pro Arg Met Glu
100 105 110
Glu Lys Glu Ala Leu Val Pro Xaa Gln Lys Ala Thr Asp Ser Phe His
115 120 125 130
Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro Arg
135 140 145
Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Xaa Glu
150 155 160
Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly Thr
165 170 175
His Lys Asp Xaa Leu Xaa Xaa Gly Thr Glu Ser Ser Ser His Ser Arg
180 185 190
Leu Ser Pro Arg Lys Xaa His Leu Leu Tyr Ile Leu Xaa Pro Ser Arg
195 200 205 210
Gln Leu

<210> 448
<211> 154
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -60..-1

<400> 448
Met Gly Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu
-60 -55 -50 -45
Arg Gln Arg Arg Gln Lys Leu Leu Leu Ala Gln Leu His His Arg Lys
-40 -35 -30
Arg Val Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu
-25 -20 -15
Val Arg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln
-10 -5 1
Cys Trp Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln
5 10 15 20
Ala Leu Leu Gly Val Tyr Val Ile Gln Glu Gln Ala Ala Val Lys Leu
25 30 35
Gln Ser Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met
40 45 50
Cys Asn Ala Leu Cys Leu Phe Gln Val Pro Lys Ser Ser Leu Ala Phe
55 60 65
Gln Thr Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln
70 75 80
Pro Glu Phe His Ile Glu Ile Leu Ser Ile
85 90

<210> 449
<211> 89
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -61..-1

<400> 449
Met Asn Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr
    -60   -55   -50
Glu Thr Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro
-45   -40   -35   -30
Glu Ala Arg Ser His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala
                -25   -20   -15
Leu Leu Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg
            -10   -5   1
Pro Asp Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro
    5   10   15
His Pro Cys Ala Thr Tyr Pro Pro Xaa
20   25

<210> 450
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 450
Met Arg Met Ser Leu Ala Gln Arg Val Leu Leu Thr Trp Leu Phe Thr
    -25   -20   -15
Leu Leu Phe Leu Ile Met Leu Val Leu Lys Leu Asp Glu Lys Ala Pro
-10   -5   1   5
Trp Asn Trp Phe Leu Ile Phe Ile Pro Val Trp Ile Phe Asp Thr Ile
            10   15   20
Leu Leu Val Leu Leu Ile Val Lys Met Ala Gly Arg Cys Lys Ser Gly
        25   30   35
Phe Asp Leu Asp Met Asp His Thr Ile
    40   45

<210> 451
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -34..-1

<400> 451
Met Ile Pro Leu Ile Ser His Leu Ala Glu Ala Ala Pro Pro Thr Ser
                -30   -25   -20
Trp Ser Leu Ile Ser Ser Val Leu Asn Val Gly His Leu Leu Phe Ser
            -15   -10   -5
Ser Ala Cys Ser Val Ser Leu Glu Ala Leu Ser Thr Arg Asn Ile Lys
        1   5   10
Ala Ile Ile Leu Met Lys
15   20

<210> 452
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -38..-1

<400> 452
Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn Ser Val Ala
-35 -30 -25
Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu Ser Cys Leu
-20 -15 -10
Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala Gly Thr Arg
-5 1 5 10
Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala Val Leu Trp
15 20 25
Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn Gln Trp Gln
30 35 40
His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser Ala Gln Ala
45 50 55
Ala Ile Gly Xaa His Leu Leu Leu His Pro Cys Leu Asp Ile Pro Xaa
60 65 70
Leu Pro Gly Xaa Pro Gly Pro Pro Lys
75 80

<210> 453
<211> 166
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -37..-1

<400> 453
Met Ser Thr Val Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile
-35 -30 -25
Cys Pro Ala Pro Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu
-20 -15 -10
Ser Pro Gly Ile Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp
-5 1 5 10
Tyr Pro Ala Leu Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe
15 20 25
Val Lys Gly His Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn
30 35 40
Cys Val Val Leu Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His
45 50 55
Gln Thr Arg Ser Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu
60 65 70 75
Gln Glu Lys Val Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His
80 85 90
Lys Glu Lys Arg Glu Ala Ala Lys Lys Lys Gln Glu Arg Lys Lys Arg
95 100 105
Ala Lys Glu Thr Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu
110 115 120

Ser Ser Lys Lys Val His
125

<210> 454
<211> 180
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 454
Met Gly Ile Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly
-25 -20 -15
Leu Val Thr Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg
-10 -5 1 5
Ser Arg Arg Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu
10 15 20
Leu Arg Leu Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe
25 30 35
Arg Phe Ala Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly
40 45 50
Lys His Ile Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg
55 60 65 70
Pro Tyr Thr Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu
75 80 85
Val Xaa Lys Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly
90 95 100
Gly Lys Met Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val
105 110 115
Glu Phe Xaa Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His
120 125 130
Phe Asn Ile Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg
135 140 145 150
Arg Asn Trp Glu

<210> 455
<211> 91
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -64..-1

<400> 455
Met Thr Pro Arg Ile Leu Ser Glu Val Gln Phe Ser Ala Phe Cys Pro
-60 -55 -50
Tyr Trp Thr Ile Ala Arg Ile Leu Glu Arg Val Gly Ser Ala Cys Phe
-45 -40 -35
Arg Leu Glu Leu Cys Ala Ala Ile Val Gly Tyr Phe Val Leu Asp Val
-30 -25 -20
Arg Thr Phe Leu Phe Ile Val Val Cys Val Ile Cys Val Thr Leu Asn
-15 -10 -5
Phe Pro Arg Phe Tyr Phe Leu Cys Leu Ser Ser Leu Thr Ala Phe Gly
1 5 10 15
Thr Pro Pro Ile Gly Val His Ile Pro Ser Pro

20 25

<210> 456
<211> 257
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -23..-1

<400> 456
Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Leu Xaa
-20 -15 -10
Leu Leu Leu Leu Leu Ile Ala Leu Glu Ile Met Val Gly Gly His Ser
-5 1 5
Leu Cys Phe Asn Phe Thr Ile Lys Ser Leu Ser Arg Pro Gly Gln Pro
10 15 20 25
Trp Cys Glu Ala His Val Phe Leu Asn Lys Asn Leu Phe Leu Gln Tyr
30 35 40
Asn Ser Asp Asn Asn Met Val Lys Pro Leu Gly Leu Leu Gly Lys Lys
45 50 55
Val Tyr Ala Thr Ser Thr Trp Gly Glu Leu Thr Gln Thr Leu Gly Glu
60 65 70
Val Gly Arg Asp Leu Arg Met Leu Leu Cys Asp Ile Lys Pro Gln Ile
75 80 85
Lys Thr Ser Asp Pro Ser Thr Leu Gln Val Xaa Xaa Phe Cys Gln Arg
90 95 100 105
Glu Ala Glu Arg Cys Thr Gly Ala Ser Trp Gln Phe Ala Thr Asn Gly
110 115 120
Glu Lys Ser Leu Leu Phe Asp Ala Met Asn Met Thr Trp Thr Val Ile
125 130 135
Asn His Glu Ala Ser Xaa Ile Lys Glu Thr Trp Lys Lys Asp Arg Xaa
140 145 150
Leu Glu Xaa Tyr Phe Arg Lys Leu Ser Lys Gly Asp Cys Asp His Trp
155 160 165
Leu Arg Glu Phe Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val
170 175 180 185
Ser Pro Xaa Asn Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro
190 195 200
Xaa Xaa Trp Ile Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly
205 210 215
Ile Val Leu Ile Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa
220 225 230
Xaa

<210> 457
<211> 193
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -60..-1

<400> 457
Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu Pro
-60 -55 -50 -45

```
Cys Ser Gly Gln Gln Gln Pro Phe Pro Phe Gly Ala Ser Asn Ile Pro
                -40                 -35                 -30
Leu Leu Leu Gly Arg Ser Arg Lys Val Ala Arg Gly Ala Pro Val Leu
            -25                 -20                 -15
Trp Pro Phe Leu Thr Trp Ile Asn Pro Ala Leu Ser Ile Cys Asp Pro
        -10                 -5                  1
Leu Gly Ser Cys Gly Trp Xaa Cys His Thr Ala Gln Val Pro Ala Pro
5                   10                  15                  20
Leu Gln Leu Pro Thr Ala Cys Pro Pro Leu Pro His Gly Thr Arg Ala
                25                  30                  35
Val Gly Pro Thr Pro Gly Leu Leu Pro Glu Ala Ala Ala Pro Xaa Thr
            40                  45                  50
Xaa Gly Ala Leu Ser Ser Arg Ser Arg His Trp Ser Cys Ser Ile Val
        55                  60                  65
Xaa Cys Leu His Leu His Xaa Leu Leu Ser Val Glu Thr Arg Xaa Phe
    70                  75                  80
Xaa Lys His Leu Leu Val Leu Leu Val Ala Val Ala His Ser Val Leu
85                  90                  95                  100
Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr His
                105                 110                 115
Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro Trp
            120                 125                 130
Glu
```

```
<210> 458
<211> 107
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -28..-1

<400> 458
Met Val Leu Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg
            -25                 -20                 -15
Phe Leu Ser Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser
        -10                 -5                  1
Trp Asp Val Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile
5                   10                  15                  20
Arg Ala Val Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys
                25                  30                  35
Val Glu Phe Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val
            40                  45                  50
Tyr Ser Leu Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu
        55                  60                  65
Ala Glu Arg Lys Ser Pro Glu Ile Ser Trp Gly
    70                  75
```

```
<210> 459
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -13..-1
```

<400> 459
```
Met Leu Val Leu Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr
            -10                 -5                  1
Leu Ala Pro Gln Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr
    5                   10                  15
Asp Gly Ile Phe Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys
20                  25                  30                  35
Met Asn Glu Phe Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr
                40                  45                  50
Ala His Ser Glu Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg
            55                  60                  65
Met Xaa Thr Val Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg
        70                  75                  80
Thr Glu Phe Gln Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln
    85                  90                  95
Phe Leu Ile Pro Asn Leu Ala Leu Asn
100                 105
```

<210> 460
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 460
```
Met Lys Val Gly Val Leu Trp Leu Ile Ser Phe Phe Thr Phe Thr Asp
        -15                 -10                 -5
Gly His Gly Gly Phe Leu Gly Val Ser Trp Cys Tyr Val Ser Tyr Leu
    1               5                   10                  15
Phe Ser Thr Asn Ser Pro Leu Ser Phe Arg Arg Ile
                20                  25
```

<210> 461
<211> 109
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -13..-1

<400> 461
```
Met Cys Leu Leu Thr Ala Leu Val Thr Gln Val Ile Ser Leu Arg Lys
            -10                 -5                  1
Asn Ala Glu Arg Thr Cys Leu Cys Lys Arg Arg Trp Pro Trp Xaa Pro
    5                   10                  15
Ser Pro Arg Ile Tyr Cys Ser Ser Thr Pro Cys Asp Ser Lys Phe Pro
20                  25                  30                  35
Thr Val Tyr Ser Ser Ala Pro Phe His Ala Pro Leu Pro Val Gln Asn
                40                  45                  50
Ser Leu Trp Gly His Pro Leu His Gly Cys Ser Trp Gln Cys His His
            55                  60                  65
Pro Gln Gly Gln Asn Leu Gln Pro Ala Ser Leu Xaa Thr His Leu Ser
        70                  75                  80
Lys Pro Lys Arg His Phe Xaa Lys Lys Xaa Cys Gln Ala
```

```
    85                  90                  95


<210> 462
<211> 143
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -41..-1

<400> 462
Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val Glu Met Val Gln Ala
    -40                 -35                 -30
Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu Glu Gly Ile Leu Ile
-25                 -20                 -15                 -10
Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr Tyr Lys Leu Gln Glu
                -5                  1               5
Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu Leu Ile Glu Glu Trp
        10                  15                  20
Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys Asp His Pro Ala Leu
    25                  30                  35
Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His Lys Thr Val Val Asn
40                  45                  50                  55
Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn Phe Leu Gly Leu Leu
                60                  65                  70
Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala Ser Leu Lys Lys Tyr
            75                  80                  85
Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr Gly Thr Phe Glu
        90                  95                  100


<210> 463
<211> 232
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<400> 463
Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val
-30                 -25                 -20                 -15
Ser Val Ala His Ala Leu Ser Leu Pro Ala Glu Ser Tyr Gly Asn Xaa
                -10                 -5                  1
Xaa Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu
        5                   10                  15
Val Tyr Tyr Lys Leu Ile Ser Ser Val Asp Pro Gln Phe Leu Lys Leu
    20                  25                  30
Thr Lys Val Asp Asp Gln Ile Tyr Ser Glu Phe Arg Lys Asn Phe Glu
35                  40                  45                  50
Thr Leu Arg Ile Asp Val Leu Xaa Pro Glu Xaa Leu Lys Ser Glu Ser
                55                  60                  65
Ala Lys Glu Pro Pro Gly Tyr Asn Ser Leu Pro Leu Lys Leu Leu Gly
            70                  75                  80
Thr Gly Lys Ala Ile Thr Lys Leu Phe Ile Ser Val Phe Arg Thr Lys
        85                  90                  95
Lys Glu Arg Lys Glu Ser Thr Met Glu Glu Lys Lys Glu Leu Thr Val
```

```
    100                     105                     110
Glu Lys Lys Arg Thr Pro Arg Met Glu Glu Arg Lys Glu Leu Ile Val
115                 120                     125                 130
Glu Lys Lys Lys Arg Lys Glu Ser Thr Glu Lys Thr Lys Leu Thr Lys
                135                 140                     145
Glu Glu Lys Lys Gly Lys Lys Leu Thr Lys Lys Ser Thr Lys Val Val
            150                 155                     160
Lys Lys Leu Cys Lys Val Tyr Arg Glu Gln His Ser Arg Ser Tyr Asp
        165                 170                     175
Ser Ile Glu Thr Thr Ser Thr Thr Val Leu Leu Ala Gln Thr Pro Leu
    180                 185                     190
Val Lys Cys Lys Phe Leu Tyr Asn
195                 200
```

<210> 464
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 464

```
Met Thr Phe Arg His Gln Asp Asn Ser Leu Met Phe Phe Ser Met Met
    -20                 -15                     -10
Ala Thr Cys Thr Ser Asn Val Gly Phe Thr His Thr Thr Met Asn Cys
-5                  1                   5                   10
Ser Leu Thr Ser Pro Val Asp Phe Lys Asp Leu Leu Arg Val Leu Leu
            15                  20                      25
Ile Lys Phe Gly Tyr Asp Arg Lys Ser Thr Ile Lys Ser
        30                  35                  40
```

<210> 465
<211> 34
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -19..-1

<400> 465

```
Met Phe Leu Lys Ser Gly Ala Gly Leu Ser Ser Cys Leu Leu Pro Leu
                -15                 -10                     -5
Cys Trp Leu Glu Arg Lys Asp His Gly Arg Arg Pro Ser Xaa His Pro
            1                   5                   10
Gly Arg
    15
```

<210> 466
<211> 215
<212> PRT
<213> Homo sapiens

<220>

<221> SIGNAL
<222> -54..-1

<400> 466
```
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa
                -50                 -45                 -40
Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val Ile Thr Leu
            -35                 -30                 -25
Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln Met Ser
        -20                 -15                 -10
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp
    -5                  1               5                   10
Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser
                15                  20                  25
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met
            30                  35                  40
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe
        45                  50                  55
Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gln Lys Val Met Phe Tyr
    60                  65                  70
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser
75                  80                  85                  90
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu
                95                  100                 105
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro
            110                 115                 120
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr
        125                 130                 135
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys Ile
    140                 145                 150
Ile Ile Arg Lys Cys Phe Ile
155                 160
```

<210> 467
<211> 27
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 467
```
Met Val Val His Leu Leu Tyr Ala His Leu Ser Phe Thr Ser Lys Arg
        -15                 -10                 -5
Ala Val Val Met Leu Lys Leu Glu Ile Thr Phe
    1                   5                   10
```

<210> 468
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -24..-1

<400> 468

```
Met Cys Ser His Ala Ser Met Ser Phe His Thr Leu Phe His Leu Leu
                -20                 -15                 -10
Phe Leu Pro His Tyr Ile Glu Thr Phe Lys Pro Gln Ser Lys His Cys
            -5                  1               5
Phe Phe Trp Ile Ala Ala Phe Leu Thr Ser Leu Leu Thr Pro Gln Ser
    10                  15                  20
Leu Gln Gly Phe His Ser Ser Leu Cys Ala Leu Arg Ser Gln His Phe
25                  30                  35                  40
Pro Ser Thr Cys Asn Cys Phe Cys Tyr Leu Thr Ile Ile Ala Leu Xaa
                45                  50                  55
Tyr Trp Asp Asn Leu
            60
```

```
<210> 469
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 469
Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser Met Leu Ser Arg Ala
    -15                 -10                 -5
Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln Gln Phe Ser Tyr Leu
1               5                   10                  15
Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly Asn Val Leu Gln Leu
            20                  25                  30
Pro Asn Phe
        35
```

```
<210> 470
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -43..-1

<400> 470
Met Thr Pro Gln Tyr Leu Pro His Gly Gly Lys Tyr Gln Val Leu Gly
            -40                 -35                 -30
Asp Tyr Ser Leu Ala Val Val Phe Pro Leu His Phe Ser Asp Leu Ile
        -25                 -20                 -15
Ser Val Leu Tyr Leu Ile Pro Lys Thr Leu Thr Thr Asn Thr Ala Val
    -10                 -5                  1               5
Lys His Ser Ile Gln Lys Asn Cys Met Xaa Leu Val Leu Gly Lys Leu
                10                  15                  20
Leu Ser Gln
```

```
<210> 471
<211> 63
<212> PRT
<213> Homo sapiens
```

<220>
<221> SIGNAL
<222> -15..-1

<400> 471
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Arg Ala Leu
-15 -10 -5 1
Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser Glu Lys His Arg
5 10 15
Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser Ala Pro Gly Ser
20 25 30
Thr Gln His Arg Arg Lys Thr Thr Arg Arg Asn Tyr Ser Ser Ala
35 40 45

<210> 472
<211> 179
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -58..-1

<400> 472
Met Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His
-55 -50 -45
Ser Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu
-40 -35 -30
Ile Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile
-25 -20 -15
Leu Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala
-10 -5 1 5
Thr Ser Ile Ser Glu Leu Cys Lys Gly Gln Glu Leu Glu Pro Ser Gly
10 15 20
Ala Gly Leu Thr Val Ala Pro Pro Gln Ala Val Ser Leu Gln Gly Ile
25 30 35
Tyr Thr Leu Pro Trp Leu Leu Gln Leu Phe His Ser Thr Ala Leu Xaa
40 45 50
Xaa Xaa Gln Gln Pro Asn Gly Ser Leu Ser Leu Asn Ile Ser Ser Ser
55 60 65 70
His Ala Pro Xaa Pro Xaa Thr Cys Thr Leu Glu Pro Gly Val Asp Pro
75 80 85
Thr Arg Xaa Val Cys Ile Asn Pro His Pro Pro Pro Pro Ile Leu Lys
90 95 100
Xaa Pro Leu Ser Pro Tyr Pro Lys Pro Gln Leu Gly Thr His Ala Gly
105 110 115
Gln Val Asn
120

<210> 473
<211> 238
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -71..-1

<400> 473
Met Xaa Xaa Phe Thr Asp Pro Ser Ser Val Asn Glu Lys Lys Arg Arg
-70 -65 -60
Glu Arg Glu Glu Arg Gln Asn Ile Val Leu Trp Arg Gln Pro Leu Ile
-55 -50 -45 -40
Thr Leu Gln Tyr Phe Ser Leu Glu Ile Leu Val Ile Leu Lys Glu Trp
-35 -30 -25
Thr Ser Lys Leu Trp His Arg Gln Ser Ile Val Val Ser Phe Leu Leu
-20 -15 -10
Leu Leu Ala Gly Leu Ile Ala Thr Tyr Tyr Val Glu Gly Val His Gln
-5 1 5
Gln Tyr Val Gln Arg Ile Glu Lys Gln Phe Leu Leu Tyr Ala Tyr Trp
10 15 20 25
Ile Gly Leu Gly Ile Leu Ser Ser Val Gly Leu Gly Thr Gly Leu His
30 35 40
Thr Phe Leu Leu Tyr Leu Gly Pro His Ile Ala Ser Val Thr Leu Ala
45 50 55
Ala Tyr Glu Cys Asn Ser Val Asn Phe Pro Glu Pro Pro Tyr Pro Asp
60 65 70
Gln Ile Ile Cys Pro Asp Glu Glu Gly Thr Glu Gly Thr Ile Ser Leu
75 80 85
Trp Ser Ile Ile Ser Lys Val Arg Ile Glu Ala Cys Met Trp Gly Ile
90 95 100 105
Gly Thr Ala Ile Gly Glu Leu Pro Pro Tyr Phe Met Ala Arg Ala Ala
110 115 120
Arg Leu Ser Gly Ala Glu Pro Asp Asp Glu Glu Tyr Gln Glu Phe Glu
125 130 135
Glu Met Leu Glu His Ala Glu Ser Ala Gln Val Arg Thr Val Gly Ile
140 145 150
Glu Asn Arg Thr Leu Tyr Phe Phe Leu Lys Arg Leu Leu Arg
155 160 165

<210> 474
<211> 178
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -37..-1

<400> 474
Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe
-35 -30 -25
Gln His Gln Gly Ala Val Glu Leu Leu Val Phe Asn Phe Leu Leu Ile
-20 -15 -10
Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe
-5 1 5 10
Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly Leu Xaa Met Gly Leu
15 20 25
Ile Leu Xaa Tyr Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Xaa Val
30 35 40
Tyr Asp Cys Val Lys Leu Thr Phe Ser Pro Ser Thr Leu Leu Val Asn
45 50 55
Ile Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln
60 65 70 75
His Xaa Ile Asn Pro His Xaa Gly Asn Ala Ile Leu Glu Lys Met Thr
80 85 90
Phe Asp Pro Xaa Ile Phe Phe Asn Val Leu Leu Pro Pro Ile Ile Phe

```
                95                      100                     105
His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly
            110                     115                     120
Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val
        125                     130                     135
Ile Gly
140
```

<210> 475
<211> 96
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 475

```
Met Ser Met Gln Phe Leu Phe Lys Met Val Ala Leu Cys Cys Cys Leu
    -20                 -15                 -10
Trp Lys Ile Ser Gly Cys Glu Glu Val Pro Leu Thr Tyr Asn Leu Leu
-5                  1               5                   10
Lys Cys Leu Leu Asp Lys Ala His Cys Val Leu Leu Thr Pro Cys Gly
            15                  20                  25
Tyr Ile Phe Ser Leu Ile Ser Pro Glu Ile Leu Lys Leu Thr Leu Ile
        30                  35                  40
Thr Leu Xaa Ile Leu Leu Ile Leu Lys Asn Leu His Leu Leu Trp Leu
    45                  50                  55
Thr Val Ser Ser Xaa Cys Val His Arg Ser Ser Ala Arg Lys Glu Lys
60                  65                  70                  75
```

<210> 476
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -24..-1

<400> 476

```
Met His Thr Phe Ala Asn Asp Arg Gly Leu Tyr Arg Ile Leu Leu Leu
                -20                 -15                 -10
His Phe Tyr Cys Leu Leu Arg Ser Ser Glu Tyr Ile Leu Gly Tyr Lys
            -5                  1                   5
Val Leu Gly Val Phe Phe Pro Ile Leu
    10                  15
```

<210> 477
<211> 113
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -27..-1

<400> 477
Met Arg Xaa Lys Trp Lys Met Gly Gly Met Lys Tyr Ile Phe Ser Leu
-25 -20 -15
Leu Phe Phe Leu Leu Leu Glu Gly Gly Xaa Thr Glu Gln Val Xaa His
-10 -5 1 5
Ser Glu Thr Tyr Cys Met Phe Gln Asp Lys Lys Tyr Arg Val Gly Glu
10 15 20
Arg Trp His Pro Tyr Leu Glu Pro Tyr Gly Leu Val Tyr Cys Val Asn
25 30 35
Cys Ile Cys Ser Glu Asn Gly Asn Val Leu Cys Ser Arg Val Arg Cys
40 45 50
Pro Asn Val His Cys Leu Ser Pro Val His Ile Pro His Leu Cys Cys
55 60 65
Pro Arg Cys Pro Glu Asp Ser Leu Pro Pro Val Asn Asn Xaa Val Thr
70 75 80 85
Ser

<210> 478
<211> 250
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

<400> 478
Met Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val
-15 -10 -5
Gly Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser
1 5 10
Gln Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly
15 20 25 30
Ala Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu
35 40 45
Lys Pro Arg Tyr Ile Xaa His Leu Gly Gln His Asn Leu Gln Lys Glu
50 55 60
Glu Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro
65 70 75
Gly Phe Asn Asn Ser Leu Pro Asn Lys Asp Xaa Xaa Asn Asp Ile Met
80 85 90
Leu Val Xaa Met Xaa Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro
95 100 105 110
Leu Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile
115 120 125
Ser Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr
130 135 140
Leu Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn
145 150 155
Ala Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln
160 165 170
Glu Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
175 180 185 190
Cys Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys
195 200 205
Ala Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val
210 215 220
Asp Trp Ile Gln Glu Thr Met Lys Asn Asn
225 230

<210> 479
<211> 151
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 479
Met Ala Ala Ser Thr Ser Met Val Pro Val Ala Val Thr Ala Ala Val
-20 -15 -10
Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile
-5 1 5 10
Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu
15 20 25
Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala
30 35 40
Leu Pro Leu Ala Glu Leu Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp
45 50 55
Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val
60 65 70 75
Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys Asn Ala Arg
80 85 90
Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val Arg Ala Ile
95 100 105
Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe Arg Thr Asn
110 115 120
Gly Lys Val Lys Ser Phe Lys
125 130

<210> 480
<211> 239
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -25..-1

<400> 480
Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu
-25 -20 -15 -10
Leu Leu Gly Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Phe
-5 1 5
Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg
10 15 20
Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe
25 30 35
Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu
40 45 50 55
Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys
60 65 70
Gln Ser Lys Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala
75 80 85
Gly Arg Gln Gln Lys Lys Lys Ile Glu Arg Xaa Xaa Xaa Xaa Leu Xaa
90 95 100

Asn Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala
    105   110   115
Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe
120   125   130   135
Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa
                140   145   150
Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys
            155   160   165
Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn
        170   175   180
Ile Gln Lys Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln
    185   190   195
Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser
200   205   210

<210> 481
<211> 208
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -92..-1

<400> 481
Met Arg Glu Pro Gln Lys Arg Thr Ala Thr Ile Ala Lys Xaa Xaa Ala
        -90   -85   -80
Xaa Glu Gly Leu Arg Asp Pro Tyr Gly Arg Leu Cys Gly Ser Glu His
    -75   -70   -65
Pro Arg Arg Pro Pro Glu Arg Pro Glu Glu Asp Pro Ser Thr Pro Glu
-60   -55   -50   -45
Glu Ala Ser Thr Thr Pro Glu Glu Ala Ser Ser Thr Ala Gln Ala Gln
                -40   -35   -30
Lys Pro Ser Val Pro Arg Ser Asn Phe Gln Gly Thr Lys Lys Ser Leu
            -25   -20   -15
Leu Met Ser Ile Leu Ala Leu Ile Phe Ile Met Gly Asn Ser Ala Lys
        -10   -5   1
Glu Ala Leu Val Trp Lys Val Leu Gly Lys Leu Gly Met Gln Pro Gly
5   10   15   20
Arg Xaa His Ser Ile Phe Gly Asp Pro Lys Lys Ile Val Thr Glu Xaa
                25   30   35
Phe Val Arg Arg Gly Tyr Leu Ile Tyr Xaa Pro Val Pro Arg Xaa Ser
            40   45   50
Pro Val Glu Tyr Xaa Phe Phe Trp Gly Pro Arg Ala His Val Glu Ser
        55   60   65
Ser Xaa Leu Lys Xaa Xaa His Phe Val Ala Arg Val Arg Asn Arg Cys
    70   75   80
Ser Lys Asp Trp Pro Cys Asn Tyr Asp Trp Asp Ser Asp Asp Asp Ala
85   90   95   100
Glu Val Glu Ala Ile Leu Asn Ser Gly Ala Xaa Gly Tyr Ser Ala Pro
                105   110   115

<210> 482
<211> 86
<212> PRT
<213> Homo sapiens

<220>

<221> SIGNAL
<222> -39..-1

<400> 482
Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg Val
-35 -30 -25
Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly Leu
-20 -15 -10
Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val Val
-5 1 5
Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe Leu
10 15 20 25
His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys Ala
30 35 40
Arg Leu Leu Thr His Trp
45

<210> 483
<211> 40
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -27..-1

<400> 483
Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
-25 -20 -15
Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
-10 -5 1 5
Leu Ser Leu Arg Ser Ala Met Ser
10

<210> 484
<211> 65
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 484
Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp Gly
-15 -10 -5
Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr Met
1 5 10 15
Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys Lys
20 25 30
Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser Ala
35 40 45
Thr

<210> 485
<211> 130

```
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -55..-1

<400> 485
Met Ala Met Trp Asn Arg Pro Xaa Xaa Xaa Leu Pro Gln Gln Pro Leu
-55                 -50                 -45                 -40
Xaa Ala Glu Pro Thr Ala Glu Gly Glu Pro His Leu Pro Thr Gly Arg
                -35                 -30                 -25
Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu Cys Gly Ile
            -20                 -15                 -10
Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser Phe Cys Thr
        -5                  1               5
Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser Glu Ala Val
10                  15                  20                  25
Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly Glu Gly Xaa
                30                  35                  40
Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu Glu Gly Arg
            45                  50                  55
Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr Gln Gly Trp
        60                  65                  70
Ala Leu
    75


<210> 486
<211> 209
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -84..-1

<400> 486
Met Val Asn Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr Gly Pro Leu
                -80                 -75                 -70
Met Leu Val Phe Thr Leu Val Ala Ile Leu Leu His Gly Met Lys Thr
            -65                 -60                 -55
Ser Asp Thr Ile Ile Arg Glu Gly Thr Leu Met Gly Thr Ala Ile Gly
        -50                 -45                 -40
Thr Cys Phe Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile Tyr Phe Leu
    -35                 -30                 -25
Ala Tyr Leu Cys Asn Ala Gln Ile Thr Met Leu Gln Met Leu Ala Leu
-20                 -15                 -10                 -5
Leu Gly Tyr Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr
                1               5                   10
Asn Ile His Leu Arg Ala Leu Phe Tyr Leu Phe Trp Leu Leu Val Gly
        15                  20                  25
Gly Leu Ser Thr Leu Arg Met Val Ala Val Leu Val Ser Arg Thr Val
    30                  35                  40
Gly Pro Thr Xaa Arg Xaa Leu Leu Cys Gly Thr Leu Ala Ala Leu His
45                  50                  55                  60
Met Leu Phe Leu Leu Tyr Leu His Phe Ala Tyr His Lys Xaa Val Xaa
                65                  70                  75
Gly Ile Leu Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro Ile Gln Arg
            80                  85                  90
Val Pro Arg Asp Ile Pro Ala Met Leu Pro Ala Ala Arg Leu Pro Thr
```

```
        95                  100                 105
Thr Val Leu Asn Ala Thr Ala Lys Ala Val Ala Val Thr Leu Gln Ser
    110                 115                 120
His
125



<210> 487
<211> 36
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 487
Met Gly Trp Gln Arg Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser
        -15                 -10                 -5
Ala His Pro Pro Gln Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp
    1               5                   10                  15
Val Gly Ile Cys



<210> 488
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -29..-1

<400> 488
Met Met Ser Ser Glu Leu Arg Arg Asn Pro His Phe Leu Lys Ser Asn
                -25                 -20                 -15
Leu Phe Leu Gln Leu Leu Val Ser His Glu Ile Val Cys Ala Thr Glu
            -10                 -5                  1
Thr Val Thr Thr Asn Phe Leu Arg His Glu Lys Ala
    5                   10                  15



<210> 489
<211> 163
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -52..-1

<400> 489
Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro Ala Pro Ser
        -50                 -45                 -40
Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg Val Arg Asp
    -35                 -30                 -25
Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly Arg Leu Glu
-20                 -15                 -10                 -5
Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg Ala Ala
```

```
                    1                   5                   10
Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val Pro Gly
        15                  20                  25
Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp Ser Trp
    30                  35                  40
Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val Arg Arg
45                  50                  55                  60
His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu Asp Pro
                65                  70                  75
Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu Gly Ser
            80                  85                  90
Met Pro Ser Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala Xaa Xaa
        95                  100                 105
Thr Arg Ser
    110
```

<210> 490
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -47..-1

<400> 490

```
Met His Gly Phe Glu Ile Ile Ser Leu Lys Glu Glu Ser Pro Leu Gly
        -45                 -40                 -35
Lys Val Ser Gln Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Ser
    -30                 -25                 -20
Pro Val Thr Trp Leu Gly Leu Leu Ser Phe Gln Asn Leu His Cys Phe
-15                 -10                 -5                  1
Pro Asp Leu Pro Thr Glu Met Pro Leu Xaa Ala Lys Gly Xaa Asn Thr
            5                   10                  15
```

<210> 491
<211> 218
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -50..-1

<400> 491

```
Met His His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys
-50                 -45                 -40                 -35
Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala
                -30                 -25                 -20
Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly
            -15                 -10                 -5
Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser
        1                   5                   10
Ser Gln Asp Leu Ser Gly Gln Thr Ala Lys Lys Tyr Ala Val Ser Ser
15                  20                  25                  30
Arg His Asn Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Xaa Lys Gln
                35                  40                  45
Xaa Leu Lys Val Ser Ser Glu Asn Ser Asn Pro Xaa Gln Asp Leu Lys
```

50 55 60
Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Lys Gly Ser Glu Asn Ser
65 70 75
Gln Pro Glu Glu Met Ser Gln Glu Pro Glu Ile Asn Xaa Gly Gly Asp
80 85 90
Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly Ser Xaa His Met Gly
95 100 105 110
Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala Asp Asn Gly Asp Asp
115 120 125
Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro Glu Ser Xaa Gln Phe
130 135 140
Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp Phe Ser Gly His Pro
145 150 155
Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln
160 165

<210> 492
<211> 216
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 492
Met Val Cys Val Leu Val Leu Ala Ala Ala Ala Gly Ala Val Ala Val
-15 -10 -5 1
Phe Leu Ile Leu Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr
5 10 15
Pro Arg Glu Ser Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His
20 25 30
Thr Thr Glu Ile Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser
35 40 45
Pro Arg His Tyr Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys
50 55 60 65
Ile Asn Ser Phe Glu Leu Xaa Arg Xaa Asp Arg Xaa Pro Ser Asn Met
70 75 80
Xaa Thr Lys Tyr Tyr Ile His Arg Ile Pro Xaa Ser Arg Glu Val Gln
85 90 95
Gln Ser Trp Pro Ser Thr Val Xaa Thr Thr Leu His Ser Met Trp Leu
100 105 110
Ser Xaa Pro Leu Ile His Arg Val Lys Pro Xaa Leu Val Leu Cys Asn
115 120 125
Gly Pro Gly Thr Cys Val Pro Ile Cys Val Ser Ala Leu Leu Leu Gly
130 135 140 145
Ile Leu Gly Ile Lys Lys Val Ile Ile Val Tyr Val Glu Ser Ile Cys
150 155 160
Arg Val Lys Thr Leu Ser Met Ser Gly Lys Ile Leu Phe His Leu Ser
165 170 175
Asn Tyr Phe Ile Val Gln Trp Pro Ala Leu Lys Glu Lys Tyr Pro Lys
180 185 190
Ser Val Tyr Leu Gly Arg Ile Val
195 200

<210> 493
<211> 134
<212> PRT

```
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -19..-1

<400> 493
Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala Gly
                -15                 -10                 -5
Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg Thr
             1               5                  10
Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Xaa His Pro Glu Ala
    15                  20                  25
Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu Ile
30                  35                  40                  45
Asp Arg Glu Asn Phe Val Asp Ile Val Xaa Ala Lys Leu Lys Ile Pro
                50                  55                  60
Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser Arg
            65                  70                  75
Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu Leu
        80                  85                  90
Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn Gly
    95                  100                 105
Asp Glu Val Lys Lys Glu
110                 115



<210> 494
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 494
Met Ala Val Thr Ala Leu Ala Ala Xaa Thr Trp Leu Gly Val Trp Gly
    -15                 -10                 -5
Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu Asn
1               5                   10                  15
Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe Gly
            20                  25                  30
Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg Ala Gln Ser Thr
        35                  40                  45
Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Ile Val His
    50                  55                  60
His Arg Glu Gly Asp
65



<210> 495
<211> 292
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -29..-1
```

<400> 495
Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe
-25 -20 -15
Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr
-10 -5 1
Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr
5 10 15
Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr
20 25 30 35
Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu
40 45 50
Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe Pro Lys Asn
55 60 65
Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Xaa His
70 75 80
Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His His Cys Val
85 90 95
Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg Xaa Phe Leu Ile
100 105 110 115
Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser
120 125 130
Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu
135 140 145
Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met Asp Thr Val Phe
150 155 160
Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu
165 170 175
Gly Phe Val Val Val Leu Xaa Phe Leu Leu Gly Gly Tyr Leu Leu Phe
180 185 190 195
Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg
200 205 210
Xaa Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro
215 220 225
Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser His Gly Leu Arg
230 235 240
Xaa Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg
245 250 255
Lys Lys Gln Glu
260

<210> 496
<211> 122
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -56..-1

<400> 496
Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg Arg Ser
-55 -50 -45
Cys Ser Arg Ser Arg Lys Arg Gln Thr Arg Arg Arg Arg Asn Pro Ser
-40 -35 -30 -25
Ser Phe Val Ala Ser Cys Pro Thr Leu Leu Pro Phe Ala Cys Val Pro
-20 -15 -10
Gly Ala Ser Pro Thr Thr Leu Ala Phe Pro Pro Val Xaa Leu Thr Gly
-5 1 5
Pro Xaa Thr Asp Gly Ile Pro Phe Ala Leu Xaa Ser Ala Ala Gly Pro
10 15 20

Phe Cys Ala Ser Phe Pro Ser Gly Xaa Leu Ser Pro Pro Gly Pro Leu
25 30 35 40
Pro Gly Val Arg Gly Leu Pro Leu Pro Ser Val Phe Tyr Ser Cys Gly
45 50 55
Ala His Pro Lys Val Leu Lys Val Ala Leu
60 65

<210> 497
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -28..-1

<400> 497
Met Leu Xaa Leu Ser Arg Ala Thr Lys Xaa Gly Arg Ala Arg Trp Leu
-25 -20 -15
Met Pro Val Ile Pro Ala Leu Gln Glu Ala Xaa Ala Gly Gly Ser Arg
-10 -5 1
Gly Gln Glu Phe Glu Thr Ser Leu Ala Asn Met Glu Thr Glu Ala Gly
5 10 15 20
Glu Leu Leu Lys Pro Arg Arg Arg Arg Leu Gln
25 30

<210> 498
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -13..-1

<400> 498
Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro
-10 -5 1
Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His
5 10 15
Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg
20 25 30 35
Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser
40 45 50
Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met
55 60 65
Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu Leu Gly
70 75 80
Arg Gln Leu
85

<210> 499
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -13..-1

<400> 499
Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro
-10 -5 1
Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His
5 10 15
Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg
20 25 30 35
Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser
40 45 50
Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met
55 60 65
Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu Leu Gly
70 75 80
Arg Gln Leu
85

<210> 500
<211> 108
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -25..-1

<400> 500
Met Ser Leu Thr Ser Ser Ser Ser Vál Arg Val Glu Trp Ile Ala Ala
-25 -20 -15 -10
Val Thr Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys
-5 1 5
Arg Phe Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His
10 15 20
Ile Gln Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp
25 30 35
Leu Gly Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe
40 45 50 55
Pro Phe Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp
60 65 70
Asn Val Gly Pro Leu Ile Ile Lys Lys Lys Glu Thr
75 80

<210> 501
<211> 183
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 501
Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
-15 -10 -5 1
Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu

```
                5                   10                  15
Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
        20                  25                  30
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
    35                  40                  45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Gly Asn
50                  55                  60                  65
Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu Leu Leu Gln Ser Cys
                70                  75                  80
Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met Ile Ile Asp Asn Arg
            85                  90                  95
Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp Thr Xaa His Val Ala
        100                 105                 110
Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly Ile Asn Leu Val Val
    115                 120                 125
Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser Asn His Ile Ala Leu
130                 135                 140                 145
Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile Cys Lys Pro Cys Gly
                150                 155                 160
Thr Gly Gln Asp Phe Lys Glu
            165
```

<210> 502
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 502

```
Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
-15                 -10                 -5                  1
Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu
            5                   10                  15
Gln Gly Xaa Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
        20                  25                  30
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
    35                  40                  45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Val Phe
50                  55                  60                  65
Arg Arg Glu Leu Ser Glu Tyr Thr Glu Xaa Leu Thr Ser Glu Pro Leu
                70                  75                  80
Xaa Ala
```

<210> 503
<211> 183
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -57..-1

<400> 503

```
Met Asp Val Thr Gly Asp Glu Glu Glu Glu Ile Lys Gln Glu Ile Asn
        -55                 -50                 -45
```

Met Leu Lys Lys Tyr Ser His His Arg Asn Ile Ala Thr Tyr Tyr Gly
    -40   -35   -30
Ala Phe Ile Lys Lys Asn Pro Pro Gly Met Asp Asp Gln Leu Trp Leu
-25   -20   -15   -10
Val Met Glu Phe Cys Gly Ala Gly Ser Val Thr Asp Leu Ile Lys Asn
                -5   1   5
Thr Lys Gly Asn Thr Leu Lys Glu Glu Trp Ile Ala Tyr Ile Cys Xaa
        10   15   20
Glu Ile Leu Arg Gly Leu Xaa His Leu His Gln His Lys Val Ile His
    25   30   35
Arg Xaa Ile Lys Gly Gln Asn Val Leu Leu Thr Glu Asn Ala Glu Val
40   45   50   55
Lys Leu Val Asp Phe Gly Xaa Xaa Ala Gln Leu Asp Arg Thr Val Gly
                60   65   70
Arg Xaa Asn Thr Phe Ile Gly Thr Pro Tyr Trp Met Ala Pro Xaa Val
            75   80   85
Ile Ala Cys Asp Glu Asn Pro Xaa Ala Thr Tyr Asp Phe Lys Xaa Asp
        90   95   100
Leu Trp Ser Leu Gly Ile Thr Ala Ile Glu Met Ala Glu Gly Leu Pro
    105   110   115
Leu Ser Val Thr Cys Thr Pro
120   125

<210> 504
<211> 140
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -14..-1

<400> 504
Met Phe Leu Thr Ala Leu Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln
                -10   -5   1
Trp Ile Gly Lys His Arg Arg Pro Arg Phe Val Ser Leu Arg Ala Lys
        5   10   15
Gln Asn Met Ile Arg Arg Leu Glu Ile Glu Ala Glu Asn His Tyr Trp
    20   25   30
Leu Ser Met Pro Tyr Met Thr Arg Glu Gln Glu Arg Gly His Ala Ala
35   40   45   50
Leu Arg Arg Arg Glu Ala Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser
                55   60   65
Lys Phe Pro Pro His Arg Phe Ile Ala Asp Gln Leu Asp His Leu Asn
            70   75   80
Xaa His Gln Glu Met Val Leu Ile Leu Ser Arg His Pro Trp Ile Leu
        85   90   95
Trp Ile Thr Glu Leu Thr Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys
    100   105   110
Ser Leu Cys Glu Asn Glu Leu Trp Thr Ser Leu Tyr
115   120   125

<210> 505
<211> 59
<212> PRT
<213> Homo sapiens

<220>

<221> SIGNAL
<222> -14..-1

<400> 505
Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg Leu His
-10 -5 1
Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser Arg Asn
5 10 15
Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser Gln Thr
20 25 30
Gly His Met Arg Met Ala Ala Leu Leu Pro Gln
35 40 45

<210> 506
<211> 101
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -36..-1

<400> 506
Met Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val Ser His Ala Arg
-35 -30 -25
Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu Asn Leu Leu Ile
-20 -15 -10 -5
Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr Ser Leu Leu Arg
1 5 10
Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu Ile Leu Phe Cys
15 20 25
Asn Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg Xaa Xaa Leu Gly
30 35 40
Arg Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu Lys Ala Asn Xaa
45 50 55 60
Ala Ala Ser Xaa Gln
65

<210> 507
<211> 341
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -55..-1

<400> 507
Met Arg Lys Val Val Leu Ile Thr Gly Ala Ser Ser Gly Ile Gly Leu
-55 -50 -45 -40
Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His Leu Cys
-35 -30 -25
Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala Ala Leu
-20 -15 -10
Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val Asp Val
-5 1 5
Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys Gln Arg
10 15 20 25

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Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met Pro Asn
                30                  35                  40
Pro Gln Leu Asn Ile Lys Ala Leu Phe Phe Gly Leu Phe Ser Arg Lys
            45                  50                  55
Val Ile His Met Phe Ser Thr Ala Glu Gly Leu Leu Thr Gln Gly Asp
        60                  65                  70
Lys Ile Thr Ala Asp Gly Leu Gln Glu Val Phe Glu Thr Asn Val Phe
    75                  80                  85
Gly His Phe Ile Leu Ile Arg Glu Leu Glu Pro Leu Leu Cys His Ser
90                  95                  100                 105
Asp Asn Pro Ser Gln Leu Ile Trp Thr Ser Ser Arg Ser Ala Arg Lys
                110                 115                 120
Ser Asn Phe Ser Leu Glu Asp Phe Gln His Ser Lys Gly Lys Glu Pro
            125                 130                 135
Tyr Ser Ser Ser Lys Tyr Ala Thr Asp Leu Leu Ser Val Ala Leu Asn
        140                 145                 150
Arg Asn Phe Asn Gln Gln Gly Leu Tyr Ser Asn Val Ala Cys Pro Gly
    155                 160                 165
Thr Ala Leu Thr Asn Leu Thr Tyr Gly Ile Leu Pro Pro Phe Ile Trp
170                 175                 180                 185
Thr Leu Leu Met Pro Ala Ile Leu Leu Leu Arg Phe Phe Ala Asn Ala
                190                 195                 200
Phe Thr Leu Thr Pro Tyr Asn Gly Thr Glu Ala Leu Val Trp Leu Phe
            205                 210                 215
His Gln Lys Pro Glu Ser Leu Asn Pro Leu Ile Lys Tyr Leu Ser Ala
        220                 225                 230
Thr Thr Gly Phe Gly Arg Asn Tyr Ile Met Thr Gln Lys Met Asp Leu
    235                 240                 245
Asp Glu Asp Thr Ala Glu Lys Phe Tyr Gln Lys Leu Leu Glu Leu Glu
250                 255                 260                 265
Lys His Ile Arg Val Thr Ile Gln Lys Thr Asp Asn Gln Ala Arg Leu
                270                 275                 280
Ser Gly Ser Cys Leu
            285
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<210> 508
<211> 108
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -42..-1

<400> 508

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Met His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala
        -40                 -35                 -30
Ile Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe
    -25                 -20                 -15
Asp Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Ala Ile Ile
-10                 -5                  1                   5
Leu Gln Xaa Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser
            10                  15                  20
Ala Ile Tyr Ala Ser Gln Thr Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys
        25                  30                  35
Gly Asp Gly Gly Ser Gly Ser Lys Gly Arg Pro Xaa Xaa Gln Thr Glu
    40                  45                  50
Xaa Phe Leu Cys Ile Ser Lys Pro Ser Ser Phe Leu
55                  60                  65
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<210> 509
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -26..-1

<400> 509
Met Glu Glu Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys
    -25                 -20                 -15
Thr Asn Gln Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala
-10                 -5                  1               5
Ser Val Arg Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser
            10                  15                  20
Lys His Leu Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp
        25                  30                  35
Phe Thr Phe Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu
    40                  45                  50



<210> 510
<211> 158
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -44..-1

<400> 510
Met Ala Gly Phe Leu Asp Asn Phe Arg Trp Pro Glu Cys Glu Cys Ile
                -40                 -35                 -30
Asp Trp Ser Glu Arg Arg Asn Ala Val Ala Ser Val Val Ala Gly Ile
            -25                 -20                 -15
Leu Phe Phe Thr Gly Trp Trp Ile Met Ile Asp Ala Ala Val Val Tyr
        -10                 -5                  1
Pro Lys Pro Glu Gln Leu Asn His Ala Phe His Thr Cys Gly Val Phe
5                   10                  15                  20
Ser Thr Leu Ala Phe Phe Met Ile Asn Ala Val Ser Asn Ala Gln Val
                25                  30                  35
Arg Gly Asp Ser Tyr Glu Ser Gly Cys Leu Gly Arg Thr Gly Ala Arg
            40                  45                  50
Val Trp Leu Phe Ile Gly Phe Met Leu Met Phe Gly Ser Leu Ile Ala
        55                  60                  65
Ser Met Trp Ile Leu Phe Gly Ala Tyr Val Thr Gln Asn Thr Asp Val
    70                  75                  80
Tyr Pro Gly Leu Ala Val Phe Phe Gln Asn Ala Leu Ile Phe Phe Ser
85                  90                  95                  100
Thr Leu Ile Tyr Lys Phe Gly Arg Thr Glu Glu Leu Trp Thr
                105                 110



<210> 511
<211> 130
<212> PRT
<213> Homo sapiens
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<220>
<221> SIGNAL
<222> -28..-1

<400> 511
Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu
-25 -20 -15
Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu
-10 -5 1
Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu
5 10 15 20
Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu
25 30 35
Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser
40 45 50
Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu
55 60 65
Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu
70 75 80
Thr Asp Thr Gly Ser His Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly
85 90 95 100
Ile Trp

<210> 512
<211> 199
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -62..-1

<400> 512
Met Ser Gln Arg Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg
-60 -55 -50
Xaa Leu Ile Glu Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys
-45 -40 -35
Val Leu Pro His Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val
-30 -25 -20 -15
Asn Ser Ile Leu Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys
-10 -5 1
Ala Ser Lys His Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu
5 10 15
Leu Ala Thr Tyr Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro
20 25 30
Val Gln Ser Asn Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys
35 40 45 50
Thr Ile Gly Asn Asn Gly Asn Gln Ser His Lys Met Thr Thr Ser Arg
55 60 65
Cys Val Arg Leu Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val
70 75 80
Trp Ile Ser Glu Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr
85 90 95
Met Pro Thr Trp Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg
100 105 110
Ile Glu Asn Phe Lys Ser Gly Val Asp Ala Xaa Ser Ser Tyr Phe Lys
115 120 125 130
Ile Phe Lys Thr Lys His Asp
135

<210> 513
<211> 180
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -25..-1

<400> 513
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Met Asn Thr Val Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu
-25                 -20                 -15                 -10
Ser Val Met Ala Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe
                -5                  1               5
Lys Asp Arg Ser Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu
        10                  15                  20
Lys Asn Val Glu Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly
    25                  30                  35
Phe Ile Thr Phe Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp
40                  45                  50                  55
Asn Val Lys Gln Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys
                60                  65                  70
Asn Asn Ala Leu Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg
            75                  80                  85
Gly Asp Asn Pro Lys Leu Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe
        90                  95                  100
Phe Phe Asp Asp Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu
    105                 110                 115
Thr Leu Ser Trp Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val
120                 125                 130                 135
Thr Gly Ser Gly His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile
                140                 145                 150
Thr Lys Ser Tyr
            155
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<210> 514
<211> 120
<212> PRT
<213> Bos taurus

<400> 514
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Met Met Thr Gly Arg Gln Gly Arg Ala Thr Phe Gln Phe Leu Pro Asp
1               5                   10                  15
Glu Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro Arg Leu Ala
            20                  25                  30
Phe Val Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp Asn Ala Ile
        35                  40                  45
Arg Arg Arg Pro Val Leu Leu Ala Gly Leu His Arg Gln Leu Leu Tyr
    50                  55                  60
Ile Thr Ser Phe Val Phe Val Gly Tyr Tyr Leu Leu Lys Arg Gln Asp
65                  70                  75                  80
Tyr Met Tyr Ala Val Arg Asp His Asp Met Phe Ser Tyr Ile Lys Ser
                85                  90                  95
His Pro Glu Asp Phe Pro Glu Lys Asp Lys Lys Thr Tyr Gly Glu Val
            100                 105                 110
Phe Glu Glu Phe His Pro Val Arg
        115                 120
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<210> 515
<211> 1082
<212> DNA
<213> Homo sapiens

<400> 515
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cgcagcccga agattcacta tggtgaaaat cgccttcaat acccctaccg ccgtgcaaaa 180
ggaggaggcg cggcaagacg tggaggccct cctgagccgc acggtcagaa ctcagatact 240
gaccggcaag gagctccgag ttgccaccca ggaaaaagag ggctcctctg ggagatgtat 300
gcttactctc ttaggccttt cattcatctt ggcaggactt attgttggtg gagcctgcat 360
ttacaagtac ttcatgccca agagcaccat ttaccgtgga gagatgtgct tttttgattc 420
tgaggatcct gcaaattccc ttcgtggagg agagcctaac ttcctgcctg tgactgagga 480
ggctgacatt cgtgaggatg acaacattgc aatcattgat gtgcctgtcc ccagtttctc 540
tgatagtgac cctgcagcaa ttattcatga ctttgaaaag ggaatgactg cttacctgga 600
cttgttgctg ggaactgcct atctgatgcc cctcaatact tctattgtta tgcctccaaa 660
aaatctggta gagctctttg gcaaactggc gagtggcaga tatctgcctc aaacttatgt 720
ggttcgagaa gacctagttg ctgtggagga aattcgtgat gttagtaacc ttggcatctt 780
tatttaccaa ctttgcaata acagaaagtc cttccgcctt cgtcgcagag acctcttgct 840
gggtttcaac aaacgtgcca ttgataaatg ctggaagatt agacacttcc ccaacgaatt 900
tattgttgag accaagatct gtcaagagta agaggcaaca gatagagtgt ccttggtaat 960
aagaagtcag agatttacaa tatgacttta acattaaggt ttatgggata ctcaagatat 1020
ttactcatgc atttactcta ttgcttatgc cgtaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080
aa 1082

<210> 516
<211> 559
<212> DNA
<213> Homo sapiens

<400> 516
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aagcacaggg aagcagaaat gagaaacagt atcttagccc aagttctgga tcagtcggcc 180
cgggccaggt taagtaactt agcacttgta aagcctgaaa aaactaaagc agtagagaat 240
taccttatac agatggcaag atatggacaa ctaagtgaga aggtatcaga acaaggttta 300
atagaaatcc ttaaaaaagt aagccaacaa acagaaaaga caacaacagt gaaattcaac 360
agaagaaaag taatggactc tgatgaagat gacgattatt gaactacaag tgctcacaga 420
ctagaactta acggaacaag tctaggacag aagttaagat ctgattattt actttgttta 480
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aaaaaaaaaa aaaaaaaaa 559

<210> 517
<211> 110
<212> PRT
<213> Homo sapiens

<400> 517
Met Phe Cys Pro Leu Lys Leu Ile Leu Leu Pro Val Leu Leu Asp Tyr
1 5 10 15
Ser Leu Gly Leu Asn Asp Leu Asn Val Ser Pro Pro Glu Leu Thr Val
20 25 30
His Val Gly Asp Ser Ala Leu Met Gly Cys Val Phe Gln Ser Thr Glu
35 40 45

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Asp Lys Cys Ile Phe Lys Ile Asp Trp Thr Leu Ser Pro Gly Glu His
    50                  55                  60
Ala Lys Asp Glu Tyr Val Leu Tyr Tyr Tyr Ser Asn Leu Ser Val Pro
65                  70                  75                  80
Ile Gly Arg Phe Gln Asn Arg Val His Leu Met Gly Asp Asn Leu Cys
                85                  90                  95
Asn Asp Gly Ser Leu Leu Leu Gln Asp Val Gln Asp Val Glu
            100                 105                 110
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<210> 518
<211> 4544
<212> DNA
<213> Homo sapiens

<400> 518

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tcccgaatcc ttatgctgat tataacaaat ccctggccga aggctacttt gatgctgccg    180
ggaggctgac tcctgagttc tcacaacgct tgaccaataa gattcgggag cttcttcagc    240
aaatggagag aggcctgaaa tcagcagacc ctcgggatgg caccggttac actggctggg    300
caggtattgc tgtgctttac ttacatcttt atgatgtatt tggggacccct gcctacctac    360
agttagcaca tggctatgta aagcaaagtc tgaactgctt aaccaagcgc tccatcacct    420
tcctttgtgg ggatgcaggc cccctggcag tggccgctgt gctatatcac aagatgaaca    480
atgagaagca ggcagaagat tgcatcacac ggctaattca cctaaataag attgatcctc    540
atgctccaaa tgaaatgctc tatgggcgaa taggctacat ctatgctctt ctttttgtca    600
ataagaactt tggagtggaa aagattcctc aaagccatat tcagcagatt tgtgaaacaa    660
ttttaacctc tggagaaaac ctagctagga agagaaactt cacggcaaag tctccactga    720
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cttttaactt taatttccat ttcttcctaa agggagagtg agtgatatgt acagtgtttt   1560
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gtttttgtcg gtaaggcata cagccttcag aagccaacat ttttaatcaa aaacttataa   1980
aacatgatga tcattgtgaa aattctgagt tgaaggttag tttaagataa gctaacaata   2040
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tgtttttcag tattcaaata agatcaggaa gccatttttc tatgtatgaa tatgctttaa   2160
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tctactcttt ctattactgc ctttgcctgg cttgttttgt ctctttgcaa ctgattttgc   2640
aaaaaaaaat tgtagcttta aaataacagg gtctaagtat tttaaatgtg cctatttcac   2700
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gacttactag ttctcaataa aattttatta ggactataaa aaaa 4544

<210> 519
<211> 1779
<212> DNA
<213> Mus musculus

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(71) Applicant *(for all designated States except US)*: GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: BOUGUELERET, Lydie [FR/FR]; 108, avenue Victor Hugo, F-92170 Vanves (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue Victorine, F-94100 Saint-Maur (FR). DUMAS MILNE EDWARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, F-75006 Paris (FR).

(74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).

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(54) Title: EXTENDED cDNAs FOR SECRETED PROTEINS

(57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

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INTERNATIONAL SEARCH REPORT

International Application No
/IB 98/02122

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/47 C07K16/18 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E,L	WO 99 06549 A (GENSET (FR); DUMAS MILNE EDWARDS J.-B.; DUCLERT A.; LACROIX B.) 11 February 1999 (1999-02-11) L: Priority abstract page 6 - page 12 page 129 - page 133; claims Seq.ID:251 page 213 - page 214 Seq.ID:484 page 366 - page 367 ---	1-20
X	Database EMBL, entry HS695112 Accession number R50695 24 May 1995 95% identity with Seq.ID:40 nt.1-384 XP002097725 the whole document ---	2,5,8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 March 1999	27.07.99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

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International Application No
F /IB 98/02122

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 34981 A (GENSET (FR); NICOLAEVNA MERENKOVA I.; DUMAS MILNE EDWARDS J.-B.G.) 7 November 1996 (1996-11-07) cited in the application abstract ---	
A	EP 0 625 572 A (KANAGAWA ACAD OF SCIENCE AND TECHNOL FOUNDATION (JP); KATO S; SEKINE S) 23 November 1994 (1994-11-23) cited in the application abstract ---	
A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996 (1996-11-01), pages 327-336, XP002081729 cited in the application abstract ---	
A	KATO S. ET AL.: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1994, pages 243-250, XP002081364 cited in the application abstract ---	
A	WO 97 07198 A (GENETICS INSTITUTE INC (US); JACOBS K; MCCOY JM; KELLEHER K; CARLIN M) 27 February 1997 (1997-02-27) ---	
A	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993 (1993-07-30), pages 600-603, XP000673204 abstract ---	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953 abstract ---	
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application abstract ---	

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 98/02122

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
WO 9906549	A	11-02-1999	AU	8555098	A	22-02-1999
WO 9634981	A	07-11-1996	FR	2733765	A	08-11-1996
			FR	2733762	A	08-11-1996
			AU	5982996	A	21-11-1996
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			WO	9408001	A	14-04-1994
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			EP	0839196	A	06-05-1998
			EP	0851875	A	08-07-1998
			WO	9704097	A	06-02-1997

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: Claims 1-20, all partially.

   Nucleic acid comprising the sequence as in Seq.ID:40, complementary sequence or fragments, host cell containing said nucleic acid. Polypeptide as in Seq.ID:141, encoded by said polynucleotide, or fragments, method of making said polypeptide. Antibody specifically binding to said polypeptide.

2. Claims: Inventions 2-233: Claims 1-20, all partially, as far as applicable.

   Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:41-140, 242-377, and corresponding polypeptides, where invention 2 is limited to Seq.ID:41 and 142, invention 3 is limited to Seq.ID:42 and 143, ..., invention 8 is limited to Seq.ID:47 and 148, invention 9 is limited to Seq.ID:48,49,110,149,150 and 211, invention 10 is limited to Seq.ID:50 and 151, ..., invention 32 is limited to Seq.ID:72 and 173, invention 33 is limited to Seq.ID:73,74,131,174,175 and 232, invention 34 is limited to Seq.ID:75 and 176, ..., invention 233 is limited to Seq.ID:377 and 513.

   For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 98/02122

Box I Observations where certain claims were found unsearchable (Continuati n of it m 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Invention 1, Claims 1-20 partially.

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

International Application No
PCT/IB 98/02122

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LOCKHART D.J. ET AL.: "Expression monitoring by hybridization to high-density oligonucleotide arrays" BIO/TECHNOLOGY, no. 14, 14 December 1996 (1996-12-14), pages 1675-1680, XP002074420 abstract -----	18

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